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AMYOTONIA CONGENITA: A SURVEY OF THE KNOWN CASES WITH A REPORT OF THREE NEW CASES *

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SAN FRANCISCO

Since Oppenheim[1] in 1900 first described this disease, case reports have gradually accumulated until at the time of writing 115 are on record, with 27 anatomic reports, including necropsies and muscle biopsies. A mass of clinical and pathologic material of these proportions appears to be great enough to render a statistical analysis of considerable value, not only in defining the disease more precisely, but in throwing new light on the etiology and in correcting some current misconceptions.

Reviews of the literature have been frequently made by those reporting new cases. It will suffice to mention the more important of these, noting that the last fairly comprehensive study — Thorspecken's — appeared more than four years ago, and that none is based on the statistical method. Batten, in 1903, without mentioning Oppenheim's description, reported three cases under the name of "myopathy — infantile type." Kundt in 1905 described a case and reviewed the subject. Collier and Wilson in 1908 collected the twenty-six then known cases, including four new ones, and gave us the masterly description which is the classic of this subject. Rothmann in 1909, Chéné in 1910, Habermann in the same year, Griffith in 1910 and 1911, Cassirer in 1911 and Thorspecken in 1912 all made careful studies of the disease. Concetti also surveyed the literature, but his paper, besides being incomplete in many points, has the disadvantage of not being generally available to the medical public. The painstaking necropsies of Marburg, Kaumheimer, Rothmann, and Foot have added greatly to our knowledge of the histologic changes in the muscles and nervous system, and their communications contain careful reviews of special phases of the subject. Of the 115 cases reported, 29 were from

* Submitted for publication Dec. 10, 1916.
* From the Department of Pediatrics, Stanford University Medical School.
1. References will be found arranged alphabetically at the end of the article.

Germany and Austria, 21 from the British Isles, 15 from France, 25 from Italy, 1 from Holland, and 24 from America.

The following synopsis is based on a tabulation of the 115 cases reported in the literature which appear to be properly diagnosed.

DEFINITION

A disease beginning at birth or in early infancy due to a congenital developmental defect of the lower motor neuron and of the voluntary muscles, clinically characterized by weakness, hypotonia and a quantitatively diminished electrical response in the muscles, usually without disturbances of a sensation or of mentality.

ETIOLOGY

Syphilis and other infections play no part. A positive Wassermann reaction was reported but once (Gordon's incompletely reported case), and in the nine other cases this test was negative. The von Pirquet tuberculin test was three times negative; never positive.

Since the pathology of amyotonia congenita furnishes strong evidence for the hypothesis of a congenital defect, it is a matter of particular importance to scrutinize the case reports carefully for clinical evidence of *hereditary* or *reproductive defects*. All the earlier writers dismiss such evidence as accidental, or state simply that heredity plays no part. The statistical study does not justify such an inference. Thus, the fact that *quickening* was absent (6), weak (12) or retarded (2) in 54 per cent.[2] of the thirty-seven cases in which notes were made of this point and normal in only 5.4 per cent. (present, degree not noted in 40.5 per cent.) proves clinically that the disease is certainly present before birth. That the pregnancies, with but two exceptions, ran a normal course to birth at full term, indicates that incidents of gestation have little to do in producing it. Familial occurrence is found three times, and these cases are by no means atypical, the two cases reported by Sorgente having been excluded by Collier and Wilson only by reason of familial occurrence, which is obviously begging the question. Skoog's familial cases were brothers, while those of Sorgente and of Concetti were brother and sister: all were successive births. Furthermore, Silvestri records the fact that a brother of his patient was paralytic at birth, and Reiner, that his patient was one of twins, the other of which died intrapartum. The second case reported by Collier and Wilson themselves was the first of three children. The second child was said to have had "something wrong with the limbs" and the third died a few days after birth. The mother had been weak as a

2. All percentages are based on the number of cases in which we have data bearing on the particular point under discussion.

child and several members of her family presented the peculiar symptom of having difficulty in closing the eyes. A study of the patients' places in the order of birth is decidedly suggestive of the possibility of *reproductive exhaustion* as a factor in the production of the disease. Unfortunately I find notes on this point in only sixteen instances. Of these, eight, or 53 per cent., were born of the fourth or a later pregnancy.

1st child	2*	6th child	1
2nd child	3*	7th child	1
3d child	2	8th child	1
4th child	1	9th child	1
5th child	3	10th child	1

* Including Concetti's familial cases.

It is unfortunate that the ages of the parents have been so rarely recorded. In one of our cases the mother was 40 years of age and approaching the menopause. In one of Concetti's cases the father was 58 and the mother 50. In our third case the mother was 28; she had had an abortion about nine months before the birth of our patient. These facts strongly suggest an analogy between mongolism and amyotonia congenita. One of Concetti's cases seems to supply the link, having typical symptoms of amyotonia congenita and a mongolian facies. This analogy, or rather, relationship, is the more strongly suggested when some of the symptoms of mongolism are remembered, such as the tonelessness of the muscles and the hypermobility of the joints. This point will be more fully discussed in another communication, but it may be said that we have already found the typical myatonic electrical reaction in three cases of mongolism.

PATHOLOGY

Muscles.—Macroscopically, the muscles are nearly always described as pale, soft, or flabby. Foot compares the appearance to that of raw pork. Sometimes very little muscle tissue is visible. The fatty infiltration appears to be constant in the affected muscles. The degree of muscular involvement varies greatly in different muscle groups. The diaphragm has always been found normal, except in Foot's case, in which some slight abnormalities in staining properties were discovered in this muscle. The muscle fibers themselves are characteristically of diminutive size. The small fibers vary in size from those consisting of only one or a few fibrillae, as in Marburg's report, to those of nearly normal diameter (Mensi). Fibers of normal size were found to be present in most of the later necropsies (Archangelsy and Abrikosoff, Councilman and Dunn, Marburg, Strauch) and probably always occur in the less severely affected muscles. There can be little question that hypertrophied fibers do occur in some cases. The measurements made

by Collier and Holmes (diameter of fibers 100 to 150 microns) leave little doubt on this point. Hypertrophic fibers were also noted by Baudouin, Lereboullet and Baudouin, Griffith and Spiller, Archangelsky and Abrikosoff, Kaumheimer and Concetti, but exact measurements were not made. Councilman and Dunn in 1911 determined in their case that the larger fibers were actually of normal size, but appeared large by contrast with the diminutive fibers, an observation repeated and confirmed by Marburg, Foot, Skoog, and Strauch, all of whom failed to find fibers larger than the normal.

The cross striations are usually well preserved. Reyher and Helmholz found them indistinct or absent, Councilman and Dunn, absent in a few; Skoog notes that they were lost in the majority of the fibers; Strauch found them less distinct than normal, and Openshaw states that they were absent. For a full description of the finer histologic changes the paper of Foot should be consulted. Nearly all the early examinations showed an increase of the sarcolemma nuclei, which in some cases (Collier and Holmes) was described as enormous. Archangelsky was the first to note that this increase is not an increase over the normal number, but only relative to the size of the muscle fibers, an observation which has been confirmed by most of the later necropsies. Apparently regressive change in the muscle affects only the sarcoplasm which becomes reduced in volume, while the sarcolemma nuclei remain unchanged in numbers. With the exception of Archangelsky and Abrikosoff and Concetti, all observers found a striking increase in the fat and connective tissue in the muscles. This points strongly to a process of replacement, though Foot disputes this on grounds which seem to me inconclusive. True degenerative changes in the muscles are exceptional, and, in my opinion, not a part of the disease.

In the majority of cases in which a careful examination has been made, the peripheral nerves have shown deficient myelinization of the fibers, with an increase of the connective tissue of the perineurium and endoneurium. In Spiller's case the nerves are stated to have been normal. Kaumheimer found an actual decrease in the number of fibers, but no axis cylinder without its medullary sheath, and Rothmann noted that the fibers themselves were small, with distinct medullary sheaths. It seems fair to conclude that the essential defect in these nerve fibers is either an insufficient supply or a complete lack of myelin in the medullary sheath, both in the peripheral motor nerves and in the motor tracts of the cord. The defective myelinization varies greatly in extent and localization in different cases, though usually selecting the lower motor neuron, and apparently is never universal, at least in viable infants.

Degeneration has been found only exceptionally. Griffith and Spiller found the posterior tibial nerve much degenerated. Councilman and Dunn found a few degenerated fibers. Some doubt is thrown on the truth of these deductions by the fact that unless performed on perfectly fresh tissue, the Marchi stain is apt to give some discoloration of what was a normal nerve, because of postmortem changes in the myelin. Degeneration, it seems safe to conclude, is not an essential part of the amyotonic process. Changes similar to those described in the peripheral nerves are encountered to a greater degree in the anterior roots, which according to all observers excepting Spiller and Lereboullet and Baudouin, are reduced in size and contain many fibers deficient in myelin. The posterior roots, on the contrary, are practically never involved (in Rothmann's case they were somewhat atrophic at the cervical level only). Spiller and Lereboullet and Baudouin found no changes in the anterior horns, and Councilmann and Dunn note only that the cells did not appear to be reduced in number, but all the other necropsies showed striking changes here. Reduction in the number of cells was always present, and absence of the large ganglion cells is noted by Mensi, Concetti and Rothmann. The cells which did occur were sometimes misshapen, sometimes pyknotic and in one case vacuolated (Foot). Changes in the posterior horns, on the other hand, were very rarely found. Rothmann states that in his case the cells were fewer than normal. Clarke's column also appears to be spared as a rule, but Marburg, Kaumheimer and Rothmann found some changes — reduction of number or absence of large cells. The cord tracts showed only deficient myelinization, except in Kaumheimer's case, in which a few degenerated fibers were seen. The brain, cerebellum and medulla are only exceptionally involved. Reduction in the number of cells, in one case with chromatolysis, was twice found (Kaumheimer and Rothmann) in the hypoglossus nucleus; in neither case was involvement of the tongue noted clinically. Berghinz found microgyria and hypoplasia of the cerebrum and cerebellum, with a decrease in the number of the cells. Concetti found that all the layers of the cerebral cortex were reduced in volume, with fewer than the normal number of cells.

An increase of neuroglia in the cord, and in one case in a few places in the cerebrum (Kaumheimer)— apparently a replacement process analogous to that in the muscles — is noted by Marburg, Foot, Kaumheimer and Rothmann, the last named also noting an increase in the vessels. Concetti made the isolated observation that the Purkinje cells of the cerebellum were reduced in number and altered in shape.

Vascular changes have been present in several cases. Thickening of the walls, due to an increase in the adventitia, are noted by Collier and Holmes, Griffith and Spiller, Rothmann, and Skoog. Intimal

changes are usually absent, but Collier and Holmes noted some proliferation. Collier and Holmes also made the interesting observation that foci of small cells occurred at intervals around the vessels, and it is interesting that Foot also found areas of small cell infiltration in the rectus abdominis. These two observations, however, do not appear to be sufficient evidence for accepting inflammation as a factor in the disease, and the inflammation may perhaps be regarded rather as a complication. The heart, except in one instance, was normal. Griffith and Spiller found that the protoplasm of the cardiac muscle was rather granular and that there was an excess of polar pigment.

The thymus, thyroid and adrenals have been examined in a majority of the necropsies and, with but few exceptions, have been found normal. Griffith and Spiller note an absence of the chromaffinic cells in the adrenals and one observer (the reference has unfortunately been lost) found a hemorrhage in the adrenal. Baudouin found sclerosis of the thymus and thyroid.

Rigor mortis, when noted (six cases), was absent.

A point which has been too little emphasized in earlier summaries and which I think deserves emphasis is the pathologic change in the muscular nerve-endings. Of those who make notes on this point, only Archangelsky and Abrikosoff say that the nerve-endings were normal. Councilman and Dunn could find no nerve-endings in the affected muscles. Foot states that normal nerve-endings were found in the normal fibers, but that none were found in the small fibers. Rothmann observed that while the nerve fibers could be seen entering the affected muscle fibers, the end-plates were absent. Mensi was unable to find nerve-endings in his five necropsies.

A review of the necropsy findings in amyotonia congenita gives one the definite conception of a failure of the peripheral motor neuron in its entirety to develop, and strengthens the analogy to Little's disease, to which Collier has drawn attention. With the exception of two early necropsies, these changes, differing in extent and severity to be sure, have invariably been found. The writer states his opinion for what it may be worth, that the primary lesion of amyotonia congenita is a congenital hypoplasia of the lower motor neuron, believing that the muscular changes are secondary to this process, and that it will be found that the original fault is in the defective germ plasm of reproductively exhausted parents.

SYMPTOMS

The *time of onset* was not noted or not known in 10 cases. Of the remaining 105, symptoms of weakness or "paralysis" were noticed at or soon after birth in 86, or 81.9 per cent. In 2 cases they were observed during the first month, without antecedent illness; during the

second month, in 2; at 3 months in 3; at 5 months in 1; at 6 months in 4; at 11 months in 1; at 12 months in 1, and at 14 months in 1. It seems likely that the failure to note symptoms at birth may be due to faulty powers of observation on the part of the parents (as Collier and Wilson point out), or that during the first three months of life hypotonia may be masked by the physiologic weakness of early infancy. In addition to the above-mentioned cases, it was asserted in four instances by the parents that the patient was normal until after illness or some other disturbance. In one case the disease was said to have followed a diarrhea at 1 month; in another, bronchopneumonia at 7 weeks; in a third, weaning at 3 months was the ascribed cause; and in a fourth, symptoms appear to have been absent until 18 months, developing after an attack of measles.

The *sexes* are represented in the proportion of 55 males (53 per cent.) to 48 females (47 per cent.).

Distribution of Muscular Weakness.—The lower extremities are the only parts found to be always involved. The frequency of involvement of the different parts of the body is shown by the accompanying table.

TABLE SHOWING FREQUENCY OF INVOLVEMENT OF DIFFERENT PARTS OF THE BODY

	No. Cases With Involvement	No. Cases Without Involvement.	No Records.	Percentage Involved of Cases with Record.
Lower extremities	107	0	8	100
Upper extremities	79	6	30	93
Thoracic respiratory muscles*	26	3	86	90
Trunk†	73	7	35	91
Neck	65	11	39	86
Face‡	20	48	47	29
Muscles of deglutition	5	—	—	—
Abdomen§	22	—	—	—

* As shown by weak or absent thoracic respiration.

† As shown by inability to sit upright or to hold spine erect.

‡ As shown by lack of expression, or "apathetic," "inert," or "indifferent" expression.

§ "Protuberant," "weak," "soft," "atonic," "distended," "tympanitic," etc.

The inability to sit upright, so characteristic of this disease, is due partly to weakness of the muscles of the pelvic girdle, and partly to weakness of the muscles which support the spine.

Two points brought out by the statistical survey are contrary to the generally accepted view, namely, the not unusual involvement of the muscles of the face and others supplied by the cranial nerves, and of the intercostals. That the muscles of mastication and deglutition are usually spared is undeniable, and, on the whole, the facial muscles show less evidence of weakness than those of the trunk and extremities. It must, however, be remembered that none of the so-called muscles of

expression are called on for work proportionally as great as that thrown on those of the extremities and trunk which also have to act against gravity, and that, since it is rare for any of the muscles to be completely unable to perform voluntary movements, it is possible that the same degree of involvement would find less expression in the facial muscles than in others. Involvement of the muscles of deglutition, which are supposed to be invariably spared, was specifically mentioned as present in 5 cases. Other instances of involvement of muscles innervated by the cranial nerves are supplied by the occurrence of nystagmus in 3 cases, of strabismus in 4, and of ptosis in 1. As regards involvement of the intercostals, the statistics practically refute the statement of Collier and Holmes (see reference to Brain, 1909, **32**, 274) that the "intercostals" act "well, as seems to be the invariable rule in this disease." In my own case the absence of thoracic breathing was evident and striking; in one other case the intercostals were specifically mentioned as being involved, in 13 others thoracic respiration was absent, and in 11 diminished; in only 3 was respiration said to be normal or negative. The diaphragm is practically never involved, though Foot describes changes in the staining properties of this muscle. It is clear that nearly any muscle may be involved in this disease, though individual cases vary greatly from one another in the distribution of weakness.

The *sphincters* have never been found abnormal, though sphincter involvement is difficult to determine in early infancy. Although *atrophy* in the sense of diminished muscular volume resulting from a retrograde process is usually stated to be absent in amyotonia congenita, the muscles are small, infiltrated with fat and the individual fibers are much less than normal in size. Atrophy as such was noted in two cases, one of which is classed by Griffith as doubtful.

Tendon Reflexes.—I have taken the knee-jerks as representative of these, though in some instances they are grouped with other reactions and reported simply as tendon reflexes. They were tested in 94 cases and were absent in 69, or 73.4 per cent.; diminished in 17, or 18.1 per cent.; present, degree not noted, in 5, or 5.3 per cent., and normal in 2, or 2.1 per cent. In one case they returned after an absence of five years. They were therefore present in 26.6 per cent. of the cases, and it is unjustifiable, contrary to the usual belief, to exclude the diagnosis of amyotonia congenita because of the presence of the patellar reflex. The other tendon reflexes such as the biceps, triceps and achilles jerks are also frequently absent.

The *superficial reflexes* are so variously reported that for statistical purposes they are best grouped, with the understanding that probably in most cases only the abdominal were tested. They were present in

20, or 50 per cent., of those in which records are at hand; absent in 20, or 50 per cent. In 2 cases the upper abdominal reflexes were present and the lower absent. In 1 they were described as "sluggish."

The Babinski, Oppenheim and Gordon reflexes were found present a few times, but nearly always before the walking age and were therefore of little significance. *Sensation* was normal in forty-four, or 91.7 per cent. of cases of which we have data. In one the pain sense, and in one "sensation" was doubtfully diminished. In only one instance was there a fairly definite history of diminution of sensation, and at a later examination it was found normal. To the almost invariable rule of normal sensation there is one exception, frequently commented on by observers, namely, the remarkable lessening of sensitiveness to the discomfort caused by strong faradic currents, a point which appears to be of considerable diagnostic significance.

Electrical Reactions. — The "myatonic reaction" of Collier and Wilson consists in a quantitative diminution of electrical irritability without the qualitative changes of degeneration. It is of all degrees of intensity, varying from a slight diminution of faradic irritability to absence of reaction to both forms of current. In the eighty-two cases of which we have notes, 82.9 per cent. showed the myatonic reaction, 6.1 per cent. were said to be normal, and 4.9 per cent. "apparently normal," the rest being too imperfectly reported to classify.

		Per Cent.
Reaction to galvanic and faradic both absent	4	4.9
Reaction to galvanic and faradic both diminished	40	48.8
Reaction to faradic absent	7	8.5
Reaction to faradic diminished	16	19.5
Reaction "myatonic in character"	1	1.2
		82.9

The reaction of degeneration was found only once, and here only "a few days before death."

I believe that the myatonic reaction will be found in every case of true amyotonia in which a careful examination of all the muscle groups is made by correct methods. It is, however, frequently present in differing degrees in different muscles in the same patient, and is often absent except in one or two groups of muscles.

The *intelligence* in amyotonia is usually normal. It was so found in 77.8 per cent. of the forty-five cases with notes on this point. That this is by no means a rule without exceptions is proved by the fact that 6.7 per cent. were said to be "backward," 4.4 per cent. were "impaired" mentally; that 2.2 per cent. were "dull," 4.4 per cent. "retarded," 2.2 per cent. idiotic, and 2.2 per cent. mongolian, making a total for deficient mentality of 22.2 per cent.

Abnormal mobility of the joints is one of the most constant symptoms of the disease, having been absent in only three of the fifty cases in which we have data on this point. It was found in the wrist five times, in the ankle four times, in the fingers, elbows and shoulders and hips each twice; in the knees once and in "all the joints" once. In the wrists the hypotonia is shown by the flail-like motion of the hands when the forearm is shaken, and in the feet by the extreme dorsiflexion which is possible. Data on the particular joints involved are decidedly incomplete.

Involvement of the heart muscle and of the involuntary muscle might be imagined as a possibility, but has never been reported. It was thought of in our case (J. C.) as a possible factor in the severe constipation with the formation of fecal impaction in the large intestine, but we finally came to the conclusion that the combination of extreme inactivity and hypotonia of the abdominal wall sufficiently explained the phenomenon. The blood pressure has been determined only in this one case (to my knowledge) and was slightly below normal (systolic 75). An electrocardiographic tracing was taken in this case also (Fig. 1), to determine the state of the heart muscle, with negative results.

Vasomotor disturbances are very infrequent. In one case marked dermographia was present and in another cold, blue extremities and frequent chilblains were recorded.

In two cases a firm edema of the face and extremities was found, and in one case the skin of the legs showed a marked thickening.

The *pad feet* described by Collier and Wilson as typical of the disease are rarely mentioned. They are well shown in the accompanying photograph (Fig. 5). *Flat feet,* resulting undoubtedly from the hypotonia of the calf muscles is mentioned twice and, judging by the frequency of involvement of the muscles of the calves and feet, occurred probably in more. *Contractures* were noted as present in 27 cases, or 81.8 per cent., and absent in 6 per cent. The hamstrings (noted as contracture of the knee, 5 times) are the most frequent seat of contractures, being mentioned no less than 10 times; next in frequency are the flexors of the thigh (5 times). The adductors of the thighs and the supinators of the forearm showed contracture in 3 cases. Contractures of the elbows, ankles, calves, and feet each occurred twice, and of the sternocleidomastoid and the biceps each once.

Special Senses.—Faulty *vision* and *hearing* were noted in one case, which also showed optic atrophy. The latter lesion was also found present in another instance. *Athetoid movements* are found twice noted, and "tremor" once. Athetoid movements are very readily confused with the physiologic movements of the hands in infancy. *Con-*

vulsions occurred four times, usually shortly before death, but sometimes as an event in early life. *Concomitant congenital defects* have been found in several cases and may be considered as affording corroboration of the theory of a developmental or germ plasm defect in the etiology of this disease. Congenital hernia occurred once, and congenital clubfoot three times. One patient had congenital (?) dislocations of the hip and thumb, and a malformation of the knee. A rudimentary penis associated with cryptorchidism was present in one case. Hemophilia was once noted.

Bones.—The bony changes which sometimes occur in amyotonia congenita usually appear to be secondary to hypotonia or due to lack of muscular support and activity. Thus, deformities of the chest were found eleven times. In one case the long bones were small and easily bent; in one case they were "atrophic," the femur being one half its normal size as shown by the Roentgen ray. In my case the bones showed medullary thinning with an apparent density of the cortex, like the changes in atrophy of disuse. In one case the Roentgen ray showed that the bones were "normal," but "undeveloped from want of use."

Moderate evidences of rickets were found five times, a rather low figure considering the frequency of this disease in the hospital class of patients. *Malocclusion* of the jaws was twice noted.

Metabolism.—Gittings and Pemberton have published the results of metabolic experiments made on Griffith's patient. The creatinin excretion was found to be extremely low.

PROGNOSIS

Improvement was noted in 41 cases; merely as having occurred in 30, or 67.3 per cent. of these; as being slight in 6, and marked in 5. There was no improvement in 2 cases and 3 patients became worse. Improvement in this disease is, however, only relative. It is evident from a survey of the reported cases that a certain degree of improvement may be expected in nearly every case, but it should be remembered that no case of complete recovery has yet been reported and that there appears to be a limit in every case beyond which improvement does not go. In Oppenheim's last case the patient at the age of 12 years was undoubtedly worse than at the age of 4; he could walk only with difficulty, all the muscles were still weak and he suffered severely from flat-foot. This, with the exception of Hartenberg's extraordinary case seen at the age of 50 years, is the oldest one on record, a fact which may be in itself of significance.

Respiratory infection, evidently resulting from weak thoracic expansion, is the complication which is most to be feared and most carefully guarded against, as the mortality figures will show.

Mortality and Causes of Death.—Death occurred in thirty-six cases, making a mortality of 31.3 per cent. The cause of death is given in thirty instances as follows:

	Per Cent.
Pneumonia (usually bronchopneumonia)	24, or 80.0
Bronchitis	3, or 10.0
Diphtheria	1, or 3.3
"Convulsions"	1, or 3.3
"Acute fever"	1, or 3.3

Bronchitis in infants severe enough to cause death is usually complicated by involvement of the lung proper, so that pneumonia may be held to be responsible for 90 per cent. of the deaths in amyotonia congenita.

TREATMENT

No specific treatment is available. Epinephrin was tried once, and this case showed improvement. Concetti believes that thyroid extract is valuable, and two of his cases improved after its use, combined with massage, exercise, and electricity. Exercise, massage and stimulation of the affected muscles with the faradic current are the most effective measures. Medication with one or another of the preparations of strychnin and cod liver oil is serviceable. In view of the great danger of respiratory infection, it is extremely important to keep patients in the open air, to maintain nutrition and to avoid contact with persons suffering from any complaint of this kind. Exercise can be obtained by routine passive movements, and, perhaps more practically in many instances, by giving the younger patients toys heavy enough to require some muscular effort in handling, and in the case of older patients by carefully regulated manual work. It is most important to make these patients use the voluntary power which is present to some degree in practically all the muscles, in the hope of increasing it. Patients able to walk should be guarded against flatfoot by the use of properly constructed shoes giving support to the plantar arch.

I beg to acknowledge my indebtedness to the reviews of Collier and Wilson and of Griffith which have been freely used in compiling this paper. I wish to thank Dr. Walter F. Schaller for the electrical and general neurologic examinations of the new cases herewith reported, Dr. Roland Tupper for the electrocardiographic record of Case 3, and Dr. W. W. Boardman for the radiographic examinations.

CASE REPORTS FROM THE CHILDREN'S CLINIC OF STANFORD UNIVERSITY MEDICAL SCHOOL

Reports of the following cases from the Children's Clinic of Stanford University Medical School have not been previously published.

CASE 1.—J. P., boy, aged 29 months; first seen Oct. 26, 1914; complaint, weakness.

Family History.—The parents have been married six years. The patient represents the third pregnancy. Within eight months before his conception the mother had two miscarriages.

Birth: Full term; instrumental delivery.

Patient's History.—He has always been weak. During the first week of life he had several convulsions, but none since that time. He was never breast fed. The first tooth was cut at 12 months. No paralysis was noticed until the mother tried to teach him to walk, when she found that the legs and back were weak and that he had difficulty in holding the head upright. He was late in learning to talk and his vocabulary is still limited to three or four words. Swallowing has been normal. He plays with his toys, using his hands with facility. He seems bright and affectionate, though easily excited. He has had none of the infectious diseases.

Examination.—There is no evidence of lues or rickets.

Head: Circumference 18.5 inches (47 cm.); oval; fontanel closed; pupils equal and react to light; no nystagmus; the eyes are slightly oblique; the teeth are normal in number, in good condition and well formed. The *hair* and *skin* are normal, without evidence of cretinism.

Muscular System: The muscles of the neck are relaxed and apparently unable to support the head properly. There is no atrophy, paralysis, spasticity, tremor or ataxia of the upper extremities, but there is some doubtful hypotonia of the fingers. He does not use the right hand voluntarily as much as the left. He grasps accurately. There is no atrophy, deformity or spasticity of the lower extremities, the muscular power of which seems to be normal in the reflex responses to stimulation. When he attempts to walk and stand there is apparent incoordination of the thighs with the trunk, the former flexing while the back goes into a flexed position with the head wobbling. He also shows a tendency to adduct the thighs when attempting to walk. He is able to take a few steps when the back is supported but otherwise cannot stand. He can sit alone but bends forward and there is pronounced weakness of the muscles of the back, so that the spine goes into a rounded kyphosis in its whole extent. There is no muscular spasm or other evidence of spinal tuberculosis.

Nervous System: The left knee-jerk is more pronounced than the right (?) but neither is exaggerated. Sensation is apparently normal throughout. The cranial nerves are normal in so far as they can be tested.

Electrical Reactions: The faradic response is relatively diminished in the deltoids, triceps muscles, erector spinae and the posterior cervical muscles. Elsewhere it is normal. The galvanic response shows a quantitative change in the deltoids and the anterior muscles of the legs. There is no reaction of degeneration.

Case 2.—Baby N., boy, aged 8 weeks.

Family History.—The mother is 40 years old and is probably approaching the menopause, since before the present pregnancy began menstruation had been absent for several months. She has a funnel pelvis and a moderate degree of nephritis. This is her second pregnancy; the first, four years ago, terminated in an abortion at the second month. Her blood is negative to the Wassermann test.

Birth: Full term; birth weight 2,150 gm.; delivered by cesarean section; blood from the cord and from the heel gave a negative Wassermann reaction.

Patient's History.—This was uneventful, except for constipation, until the baby was 7 weeks old, when the father insisted that something was wrong with the left shoulder.

Examination.—The humeri are held at right angles with the body and the hands and forearms are in excessive pronation. All movements of the shoulder joints are possible and the elbow joints are normal. Supination in both lower arms is limited, whereas pronation can be carried out to an unusual extent.

The arms cannot be fully extended; when this is attempted, the tendon of the biceps muscles becomes tense.

The lower extremities are almost completely paralyzed, the left being specially flaccid. The hypotonicity of the muscles of the calf permits marked dorsiflexion of the foot.

Electrical Reactions: With the galvanic current, 1.5-2 m.a. give a normal reaction in the calf muscles, but no reaction at all can be obtained with the faradic. The thigh muscles on the right side react with 2.5 m.a., on the left with 4 m.a. The supinator longus reacts with 2.5 m.a. In general the muscles of the upper extremity react at about 2 m.a.

CASE 3.—J. C., male, aged 30 months, was seen first, Sept. 30, 1916. Complaint: "Baby is like a bunch of rags."

Family History.—Father and mother are in good health; their ages are, respectively, 30 and 28 years. They have been married six years. There are no indications of tuberculosis or of syphilis. The first child died when one month of age, of unknown cause, and eight months later our patient was born. A third child, a boy, is now 18 months old and apparently normal.

Pregnancy: There were no prenatal disturbances. The mother does not remember whether or not she felt the prenatal movements.

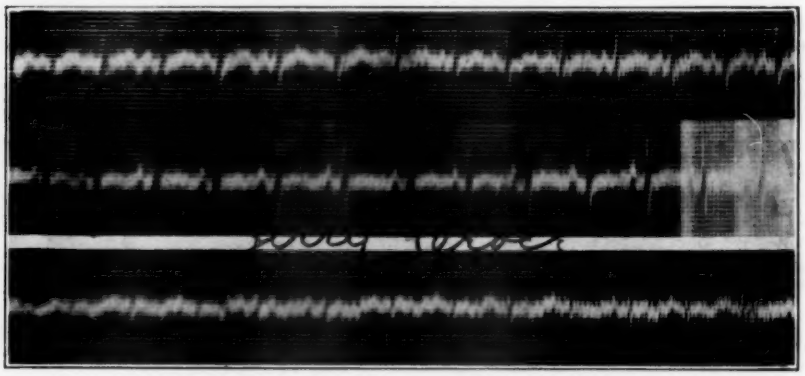

Fig. 1.—Electrocardiogram. Normal. Author's Case 3.

Birth: Born at full term. The labor was normal. The birth weight is not known.

Patient's History.—The patient was breast fed for 3 months, afterward on dilutions of cow's milk, and later on a rather careless general diet. The first tooth was cut at 6 months and the rest followed apparently at the usual intervals. The mother does not know when the anterior fontanel closed. About a year prior to being seen the boy had "pneumonia" which lasted twenty days and was followed by a good recovery. He has been obstinately constipated for the past year; he has enuresis; the mentality has been normal; at the age of 1 year he was able to speak a few words; his appetite is poor; he did not gain normally after the sixth month.

Present Illness.—His mother is sure that the weakness began at the time when she weaned the baby (at 3 months). Since then he has been weak and has never been able to sit up. He can, however, move the extremities voluntarily, though such efforts have always been weak.

Examination.—A rather poorly nourished male child, quiet and making few voluntary movements. The skin is soft and the hair fine.

Head: The anterior fontanel is closed. The suboccipito-bregmatic circumference is 47 cm. A very slight asymmetry of the skull is present, but there is

no evidence of lues or rickets. The expression is decidedly inert, but when he cries there is no apparent paralysis or weakness. The action of the orbicularis oris and palpebrarum is strong. The muscles of the tongue and of the pharynx apparently act normally. There is no ptosis or strabismus.

The pupils react promptly to light. No nystagmus can be detected. Vision is probably good. The sclerae are bluish. There are no deformities of the ears, and hearing is normally acute. There are twenty-two teeth, all in good condition. There is marked malocclusion, the lower incisors lying in a vertical plane about ¼ inch posterior to that of the upper incisors. This deformity is apparently due to a shortening and broadening of the mandible. The palatal arch is normal. The tonsils are markedly enlarged, but not inflamed. The pharynx is normal. The tongue is protruded in the median line.

Fig. 2.—Case 3, showing weakness of shoulder muscles and deformity of thorax.

Neck: The thyroid is not palpable. The thymus cannot be felt in the suprasternal notch. Both the anterior and the posterior lymph glands are palpable.

Chest: The thorax presents a marked anteroposterior flattening, with the typical sternal depression of funnel-breast. There is no rosary, but the lower ribs flare slightly and there is a suggestion of Harrison's groove. The pectorales majores appear to be somewhat atrophic. On inspiration there is a definite retraction of the intercostal spaces and of the suprasternal notch. Respiration appears to be entirely abdominal. The only abnormalities found in the examina-

tion of the lungs are a few moist râles at the right base posteriorly and perhaps slight impairment of resonance at this point. (These signs were not again heard after the first examination). No thymus dulness can be elicited.

Back: When the patient is held in a sitting posture the entire spine shows a regular, evenly distributed kyphotic convexity, without lateral curvature, which disappears when he is laid on his back. There is no angular prominence, muscular spasm or other sign of spinal tuberculosis. The deformity is evidently due to weakness of the muscles.

Heart: Dulness is present from the right border of the sternum to the midclavicular line in the fourth space. The apex impulse is felt just below and about 1 cm. inside the same line. The rate varies considerably from time to time, but on the whole is normal. The first sound is somewhat shorter and sharper than usual, giving the impression of a lack of muscular tone. The second sound is normal. There are no murmurs or accentuations.

Fig. 3.—Case 3, showing weakness of back. The head has to be supported.

Abdomen: The circumference is 43.3 to 43.7 cm. with a maximum of 0.5 cm. The contour is rounded and quite normal. There are no signs of fluid. There are several hard, rounded masses which feel as if they were directly under the abdominal wall. Their outlines are sharp and distinct. One of these is a short distance above the symphysis and another in the region of the ascending colon. Several others are felt in various parts of the lower abdomen. There is no tenderness and no spasm, the abdominal wall being flaccid and toneless. The liver and the spleen are not palpable.

Lymph-Nodes: The inguinal and axillary glands are palpable, but small and discrete. The epitrochlears are not palpable.

Extremities: The great toes are held in rather sharp dorsiflexion. The feet are long, with peculiarly puffy plantar pads, which do not pit on pressure. The

pads extend behind the os calcis, increasing the length of the foot considerably (Fig. 5). The metacarpo-phalangeal joint of the thumbs is very loose, admitting extreme hyperextension at this joint. The index finger of the right hand is constantly held in hyperextension nearly at right angles to the dorsum of the hand. The elbow joint can be slightly hyperextended and the wrists are so loose that the hands can be flapped to and fro like a flail. The hips are slightly hypermobile. The quadriceps femoris appears to be nearly powerless. The ankles permit dorsiflexion of the foot to an acute angle, but the dorsum of the foot cannot be approximated to the shin. The muscles throughout the body are soft. The upper arm muscles are small and probably atrophic, though no local wasting is apparent. The hands are long and gracile, with rather large hypothenar pads. The legs have the normal contour and are neither atrophic nor hypertrophic. All the muscles of the extremities feel soft, very much as though the soft parts consisted of fat. There is no fibrillation. The cervical muscles fail to support the head until it is lifted upright. When this is done the head does

Fig. 4.—Case 3, showing weakness of extensors of left wrist, causing "flail wrist." The right wrist is much stronger.

not drop, but is held unsteadily. There are no *contractures*, except possibly of the adductors of the thigh, which become taut when the legs are abducted (Fig. 6).

Reflexes: No patellar, achilles, biceps, triceps, wrists, jaw or knee-jerks could be obtained. The upper abdominal reflexes are prompt, but the lower ones could not be obtained. The Babinski, Oppenheim and Gordon signs were positive.

Electrical Reactions: These were performed by Dr. Schaller who made the following note: "In the anterolateral group of the legs and in the muscles of the forearm the faradic response is perhaps somewhat, but not markedly, slowed. In the calf muscles and the thigh muscles the faradic response is markedly slowed. In the arm muscles proper, including the deltoid, there is a marked slowing of the contraction. By slowing is meant that a greater amount of

current is required to produce a contraction. To the galvanic current the relative excitability of the muscles is the same as to the faradic current. There is no reaction of degeneration, but a diminished quantitative change. In general, hypoexcitability to both forms of current is more marked in the proximal than in the distal muscle groups. This electrical behavior is what would be expected in myatonia."

Urine: Specific gravity, 1.015; albumin, faint trace; sugar, none; casts, none; otherwise negative.

Blood (Oct. 11, 1916): Red blood cells, 5,064,000; hemoglobin, 85 per cent. (Sahli); color index, 0.85; white blood cells, 11,800; polymorphonuclears, 37 per cent.; lymphocytes, 60 per cent.; large mononuclears, 2 per cent.; eosinophils, 0; transitionals, 1 per cent.; (200 cells counted).

Fig. 5—Case 3, showing long, broad feet with marked increase of plantar subcutaneous tissue; so-called "pad feet."

Stool (Oct. 10): Small, fair consistency, greenish; considerable mucus and a small amount of blood; negative for formed elements. Wright stain shows many cocci and bacilli; no long chains, no pus cells. Sudan III shows excess of neutral fat; no fatty acids or soaps, by carbolfuchsin. Gram stain, shows gram-positive cocci in short chains, gram-positive and gram-negative cocci and bacilli. Lugol's iodin showed no starch.

A culture from the throat, taken as a routine precaution, was negative for diphtheria bacilli. The von Pirquet and Wassermann tests were negative.

The systolic blood pressure, taken Oct. 13, 1916, was 78 mm. (palpation); the diastolic could not be obtained.

An *electrocardiographic* tracing showed no abnormality.

Roentgenograms of the hands, forearms, thorax and spine, and of the legs were made by Dr. Boardman, who reported as follows:

"Examination shows no gross abnormalities in bony development. There is a medullary thinning of the long bones, with a resulting striking density in the cortex, giving the appearance of a penciled outline; this is especially seen

in the short bones of the hand and is also seen in the carpal bones. There is no delay in the bony development as evidenced by the appearance of the centers of ossification. The whole picture is similar to that seen in the atrophy of disuse in adults, and I should be inclined to ascribe the appearance in this case to a similar process."

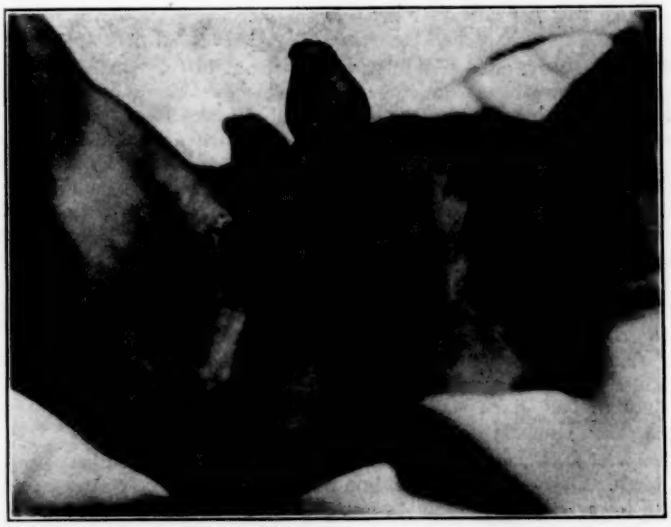

Fig. 6.—Case 3, showing retention of tonus in adductors of thighs.

Fig. 7.—Case 3, radiograph showing rarefaction of the medulla and density of the cortex in the bones of the hand.

The abdominal masses, which had given rise to various diagnostic conjectures, disappeared after a series of soapsuds enemas. Scybalous masses, some of them as large as a hen's egg, very hard, of putty color and an extremely offensive putrefactive odor, were evacuated. A few days later the child developed a

colitis with frequent passages of blood-stained mucus. This cleared up satisfactorily after a course of protein milk.

The condition of the musculature during the patient's short stay in the hospital remained stationary.

He has not yet been long enough under observation to permit any conclusions as to the progress of the disease.

ABSTRACTS OF CASES[3]

Zappert, O.—Boy, aged 6½ months. Onset at birth. Birth normal. Since birth has not been able to move legs. Great flaccidity of entire musculature. Cannot lift head. Arms somewhat elevated on shoulders, flexed at elbows, with the forearms in supination and the thumbs turned inwards. Legs motionless, feet in position of talipes equinus. Power of voluntary movement in arms very slight and almost absent in fingers. Tendon reflexes completely absent. Abdominal reflex absent. Abdomen distended. Respiration mainly abdominal. Paralysis of extremities somewhat more marked on right side than on left.

(Zappert leaves diagnosis undecided, but does not believe it to be poliomyelitis. This case, to which attention was called by Rothmann, seems so typical of amyotonia that I have included it in the series.)

Bernhardt, M.—Boy, aged 9 months. Premature; birth weight less than 3 pounds. Onset at fourth month. No involvement of face. Extremities weak. No response to faradic; to galvanic much diminished. Superficial and tendon reflexes not noted. Back shows kyphoscoliosis. Hypermobility present. Neck muscles weak. Unusual only in fact of prematurity.

Archangelsky, W., and Abrikosoff, A.—Girl, aged 3½ months. Onset probably at birth. Quickening present, but weak. Involvement of muscles of neck, upper and lower extremities, and trunk. Doubtful contracture of biceps. Knee-jerks absent. No response to faradic current, except in facial muscles. Marked deformity of chest. Breathing almost entirely abdominal. Abdomen distended. Marked hyperextension. Sensation normal. Birth weight 8½ pounds. Died of pneumonia. Necropsy.

Carcupino Ferrari, D.—Girl, aged 3½ months. Family history, pregnancy and birth normal. Quickening at the fourth month. At birth, weakness of all muscles including those of the neck. Active movements lacking except under strong electrical stimulation. Plantar and patellar reflexes diminished, abdominal uncertain, pharyngeal and pupillary normal. Pain and thermal sense normal. Slight improvement in two months. The baby then died of bronchopneumonia. During the last days of life there was a complete reaction of degeneration in some muscles and an incomplete in others.

Concetti, L.—1. Boy, aged 1½ months. Onset at birth. The parents are 58 and 50 years old. Quickening noted but not active. Muscle tone very deficient in all the extremities which are flaccid and permit free movement in all directions. Legs motionless. Arms in exaggerated supination and held away from trunk. Some voluntary movements of fingers and hands. Cannot sit up. Marked kyphosis. Head falls in all directions. Respiration entirely abdominal with retraction of epigastrium and suprasternal space. Abdominal muscles weak. In the face the folds are not normally distinct and there is an expression of indifference. Muscles of deglutition and of the eyes normal. Knee-jerks absent. Electrical excitability much diminished. No reaction of degeneration. Mentality normal. Marked improvement on massage and electricity. Died several months later of bronchopneumonia.

2. Boy, aged, 7 months. Second child. The first was premature and died two hours after birth. At the sixth month of pregnancy the mother noticed

3. Excluding the three cases reported in full elsewhere in this paper, and the sixty cases reviewed by Griffith, the references to which will be found in the bibliography.

that the fetal movements disappeared, returning at the eighth month, but feebly. Difficult labor. Born asphyxiated.

Infant small but with excessive fat deposit on legs and firm edema. Flaccid and relaxed and fell in a heap because of relaxation of muscles and joints. Some voluntary movements of the hands at two months. Examined by Concetti at the age of 7 months. Head dangles in all directions. Trunk goes into marked dorsal kyphosis when sitting. All the extremities flaccid, though some motions of the hands, forearms, and toes are made and there is some resistance in the abductors of the thighs. Muscles of face, eyes, and of deglutition normal. Sensation normal. Tendon reflexes absent. No atrophy. No reaction of degeneration. Testes undescended and penis rudimentary. Mentally a little below normal. Remarkable improvement on electricity, massage and thyroid extract. Died some time later of bronchopneumonia.

3. Girl, aged 8 months. Onset at birth. Family history negative. During last week of pregnancy mother noticed a progressive weakening of the fetal movements. Normal birth. Infant very small. The entire body was relaxed, the head falling in every direction, the trunks and legs flaccid, the legs motionless. Hypermobility of all joints. Voice feeble.

Seen by Concetti at 4 months. Head small with frontal and parietal bosses. Mongolian facies. Eyes oblique and almond shaped. Excessive adipose deposit and general pseudo-edema. On lower extremities and over deltoids and in supraclavicular region there are soft, elastic fat pads. Indifferent to surroundings. Does not smile. Movements of mastication normal. Muscles flaccid, not atrophic. Tendon reflexes absent. Rosary present. Large, flaccid abdomen. Marked improvement on thyroid with disappearance of pseudo-edema and fat pads and improvement of mentality (doubtful case).

4. Girl. (Patient not seen by Concetti. History obtained from parents). First child of young and healthy parents. Born in a state of flaccid immobility of all limbs. Sucked well and was abnormally fat. Died at age of 3 months of bronchopneumonia. Shortly before death she showed slight movements of the hands. (Data insufficient for definite diagnosis.)

5. Boy, aged 2 months. Brother of patient, Case 4. Quickening became weak during last month of pregnancy. Muscular flaccidity of extremities, neck, and back. Diminished thoracic expansion. Firm edema of calves, lower half of thigh and of forearms. Face a little apathetic. Sucks well. Well nourished. Weight 4,650 gm. Body length 54 cm. Improved on massage and thyroid extract. Died at age of 5 months of bronchopneumonia.

6. Boy, aged 6 months. No hereditary taint. Born flaccid and asthenic. Complete immobility of lower limbs. Condition less marked in upper extremities. Limited movements possible in forearms and hands. Trunk curved forward when sitting. Head well supported on shoulders. Reflexes absent. Muscles not atrophic but lacking in tone. Intelligence retarded. Subcutaneous fat abundant. The fetal movements were always weak, especially during the last month of pregnancy.

7. Girl, aged 4½ months. Parents young and robust. Immobility first noticed at 2 months (but parents could not say that he had moved since birth). Flaccidity of muscles of neck and back. "The signs of hypothyroidism were evident." Abdomen large and flaccid with a large umbilical hernia. There was never any attempt at laughing and very little at crying. Firm edema of calves, feet, and external side of thighs. Skin rough. Hair fine, stiff and dry. Constipapated. (Examination was not completed and the patient was lost sight of.) She died a few months later of bronchopneumonia.

Councilman, W. T., and Dunn, C. H.—Boy, aged 6 months. Onset at 3 weeks. Quickening present and normal. Involvement of upper and lower extremities, trunk and neck. No involvement of face. No contractures. Knee-jerks absent. Electrical reactions not performed. Deformities of chest. Respiration abdominal. Died. Necropsy.

Rietschl.—Sex not stated; 4 years old. Onset at birth. Improvement after treatment with faradic current (further details not given).

Schippers, J. C.—Boy, aged 2 years. Onset at birth. Main involvement in buttocks and extremities. Muscles of face, deglutition and mastication normal. Faradic and galvanic response diminished. No reaction of degeneration. Athetoid movements of fingers and toes. Marked dermographia. Babinski positive. Wassermann and von Pirquet negative. Gradual improvement after eight months.

Batten, F. E.—Boy, aged 6 years. Onset at birth (?). Involvement of muscles of upper and lower extremities and trunk. No involvement of facial muscles. Knee-jerks present. Faradic response diminished. Galvanic not noted. Marked spinal lordosis. Hypermobility of feet and hands. Sensation normal. No contractures. Improvement doubtful.

Beling, C. C.—Boy, aged 3 years. Onset at birth. Involvement of muscles of neck, upper and lower extremities, and trunk. No contractures. Wrist and elbow jerks present, knee-jerks absent. Electrical reactions "myatonic in character." Head circumference 20⅛ inches; chest circumference 29 inches. Harrison's groove. Abdomen 30 inches, protuberant. Back: marked weakness and kyphoscoliosis. Hypermobility present. Sensation: touch normal; pain sense diminished (?). Wassermann negative. Mentality normal. Improvement.

Charles, J. R.—Boy, aged 6 years. Onset at birth. Quickening felt. Involvement of arms, legs, and trunk. No involvement of muscles supplied by cranial nerves. Knee-jerks present. Triceps jerk absent. Wrist jerk present. No Babinski. Sensation normal. Faradic response diminished "in some" muscles. Flail wrists, knees, and ankles. Flat foot. Partial dislocation of wrist joints. Mentality normal. Double congenital inguinal hernia. Began to walk and talk at 2 years.

Duthoit, R.—Girl, aged 2 years. Onset at birth. Quickening at fifth month. Involvement of muscles of upper and lower extremities and trunk. No involvement of face. Tendon reflexes absent. Electrical reactions: faradic response diminished and sluggish; galvanic diminished but prompt. Involvement of intercostal muscles. Kyphosis. Hypermobility of all joints. Sensation normal. Improvement on thyroid extract.

Feer, E.—Girl, aged 4½ months. Onset at birth. Quickening noted. Involvement of muscles of upper and lower extremities and neck. No involvement of face. Tendon reflexes absent. Superficial reactions present. Faradic response diminished and sluggish. Galvanic diminished. Slight improvement. Harrison's groove present. Respiration abdominal. Abdomen very soft. Hypermobility present. Mentality normal.

*Guinon and Gaudu*cheau.—(Doubtful case.) Family history negative. Birth normal. Extreme weakness of musculature and apparently complete absence of motion. Extreme lordosis. Head in opisthotonos. Lower jaw dislocated. Slight stiffness of muscles followed by flaccidity when child was moved. Respiration abdominal. Muscles of face and pharynx uninvolved. Ptosis, nystagmus, and strabismus. Apparent deafness. Tendon reflexes absent. Skin reflexes lively. Sensation normal. No fibrillary twitchings. Electrical reactions normal.

Marburg, O.—1. Boy, aged 3 months. Onset at six weeks. Pregnancy normal. Patient was seventh child. Birth weight 3,740 gm. Involvement mainly of neck, arms and legs. Trichterbrust. Contracture of arms at elbow. Knee-jerks and abdominal reflex absent. Mentality apparently normal. Died of bronchopneumonia.

2. Girl, aged 6 years. Onset at birth. During pregnancy mother had vomiting and loss of appetite. Patient had rickets, and scarlet fever at 3 years. Involvement of arms, shoulder girdle and legs. Face and neck not involved. Contractures of elbows, ankles and adductors of the thigh. Hammer toe. Hyperextension of shoulder, wrist, and fingers. Spinal muscles not involved.

Triceps and knee-jerks absent. Sensation normal, Superficial reflexes present. Electrical responses quantitatively diminished.

Mensi, E.—1. Girl, aged 12 days. Weight 2,090 gm. Icterus. Cephalhematoma. Arms inert at side of body. Slight flexure of forearms and arm and of last four fingers. Passive movements free. No atrophy. Died of bronchopneumonia.

2. Boy, aged 4 days. Weight 2,750 gm. Edema of feet and legs. Paresis of extensors of hands. Lower extremities completely immobile; when picked up they fall inert. No spasm or atrophy. Died at 27 days of bronchopneumonia.

3. Boy, aged 2 days. Weight 2,800 gm. Complete immobility of lower extremities. Some slight movements of upper extremities and head. Joints loose. No hypertonic spasm or atrophy. Died at 2 months of bronchopneumonia.

4. Girl, aged 1½ months. Weight 2,800 gm. Immobility of upper extremities, especially left. Paresis of extensors of hand. Immobility of lower limbs. Knee-jerks absent. Plantar reflex present. Passive movements free in all joints. No spasm or atrophy. Cutaneous edema of forearms and legs. Died of bronchopneumonia.

5. Girl. Seen at birth. Weight 1,600 gm. Atony of upper extremities. When picked up the arm falls without tone. Slight movements of rotation of arm, of abduction of hand and of the shoulder, and of flexion of the forearm at the elbow. The head wobbles in all directions. The lower limbs also move, but weakly. Plantar and patellar reflexes present. No atrophy. Died at the age of 3 weeks of bronchopneumonia.

Oppenheim, H.—Boy, aged 12 years. Onset at birth. Never able to hold up head or sit erect. Late in learning to walk; then only with support. Condition stationary to the third or fourth year, after which he gradually became worse. Mentality normal. Muscles supplied by cranial nerves normal. Main involvement in legs with marked hypotonia. Contractures of flexors of knee, latissimus dorsi and biceps. Weakness in all muscle groups. Arms weak and hypotonic. Neck slightly weak. Electrical reactions show quantitative decrease. No reaction of degeneration. Abdominal reflexes absent. Sensation normal.

Snow, I. M.—Boy, aged 2 years and 9 months. One older brother mentally backward. At the age of 2 months had an illness characterized by fever, unconsciousness and retraction of the head, and anesthesia of the legs. No convulsions. Following this, the legs were tender for three weeks, and ever since they have been weak. At the age of 2 years patient could feed himself and sit erect, but the legs were weak. No absolute paralysis. Knee-jerks absent. Babinski positive. Faradic and galvanic response in all the leg muscles; sluggish in the abductors. Hypermobility of legs. No atrophy. (Case anomalous in onset, distribution, and electrical reaction.)

Thorspecken, O.—Girl, aged 4½ years. Date of onset not known. Quickening present. Involvement of muscles of neck, trunk and legs. Face not involved. Contractures of foot. Hypermobility of hips. Deformity of chest. Weakness of abdominal wall. Kyphoscoliosis. Tendon reflexes absent. Sensation, when patient was first seen, diminished; later, normal. Upper abdominal reflex present; lower, absent. Electrical reactions: faradic much diminished. Mentality normal. Wassermann negative. Roentgen ray shows atrophy of long bones, femur being one-half normal diameter. Improvement on exercise and faradization.

Bienfait.—Boy, aged 12 months. Weight 10½ kilos. Onset at birth. No voluntary movements until recently. There is now some action of extremities. Cannot sit up. Face and hearing normal. Mentality backward. Tendon reflexes weak. Abdominal reflexes absent. Improvement beginning after treatment with massage and electricity.

Concetti, L.—1. Girl, aged 3 years. Mother alcoholic. Normal pregnancy and birth. Onset at birth. Lower extremities immobile and atonic. The upper also appeared weak with limited powers of motion. For the past year she has

tried to walk but falls "like a rag." General hypotonia and flaccidity of muscles, especially of the legs. All joints relaxed. Dorsal kyphosis. Knee-jerks present but torpid. Plantar reflex flexor in type. Faradic and galvanic response both diminished. No reaction of degeneration. Constipated. Intelligence a little retarded. Some improvement after treatment with massage and electricity.

2. Girl, aged 53 days. Family history negative. The fetal movements near term were feeble. At 4 days of age it was noticed that the lower extremities were inert and that the upper were held in supination, with slight movements of the fingers and hands. No resistance to passive movements. Joints relaxed. When sitting there is a large dorsolumbar kyphosis and the head falls of its own weight. When the child is lifted by the axillae the head and neck fall on the shoulders. Tendon reflexes absent. Thorax deformed, with lateral depressions and prominence of the sternum. Abdomen large. Spleen palpable. Respiration weak and mainly abdominal. Movements of suction, deglutition, and expression and of the eyes normal. Electrical excitability diminished. No reaction of degeneration. Died at the age of 2 months of bronchopneumonia.

Cotterill.—Girl, aged 2½ years. Onset at birth. Involvement of face, neck, trunk, upper extremities, and especially lower extremities. Contracture of sternocleidomastoid muscle. Knee jerks absent. Abdominal muscles weak. Umbilical hernia. Kyphoscoliosis. Hyperextension. Sensation normal. Superficial reactions absent. Dislocation of right hip. Malformation of right knee. Partial luxation of left thumb. Gradual improvement.

Fletcher, H. M.—Boy, aged 3 years. Onset at birth. Face "expressionless." Involvement of upper and lower extremities and trunk. Hypermobility very marked. Contractures of the hamstrings. Knee-jerks "very difficult to obtain." Electrical reactions: faradic and galvanic both diminished. Superficial reactions present. Mentality normal. Wassermann negative.

Foot, N. C.—Boy, aged 3½ months. Onset at birth. Quickening noticed, but feeble. Involvement of upper and lower extremities. Knee-jerks present but diminished. Electrical reactions diminished. Respiration mainly abdominal. Abdomen tympanitic. Died. Necropsy.

Gatti, L.—Aged 3 years. Onset at birth. Flaccid paralysis of the lower extremities. Marked muscular atony. Feet plump and flat. Reflexes and electrical irritability retained. Improved.

Gordon, A.—Two cases not reported separately. Weak muscular tonus. Paretic condition of limbs and trunk, dating from birth. Loss of reflexes. Weak response to faradism and galvanism. One case shows double optic atrophy and positive Wassermann. Both unable to sit erect, but have shown improvement. In discussion, Spiller thought one case not myatonia congenita; but Gordon reasserted his diagnosis.

Hertz, A. F., and Johnson, W.—Boy, aged 3½ years. Onset at birth. Face not involved. Upper and lower extremities, trunk and neck involved. Tendon reflexes absent. Scoliosis. Hypermobility. Mentality normal. Improvement: a little stronger than two years ago.

Kaumheimer, L.—Girl, aged 3¾ months. Onset at birth. Quickening noted. Involvement of neck, upper extremities, lower extremities, and trunk. Contractures present. Tendon reflexes absent. Electrical reactions: faradic much diminished, galvanic weak. Head, circumference 41 cm. Thorax deformed; thoracic respiration poor. Abdomen protuberant. Kyphosis. Hypermobility present. Small at birth. Wassermann negative. Von Pirquet negative. Died.

Koch, George.—Child aged 1¼ years. Sex not stated. Onset at 6 months. Quickening noted. Involvement of neck, upper and lower extremities and trunk; face not involved. Knee-jerks present but diminished. Electrical reactions: faradic and galvanic both diminished, but galvanic more. Hypermobility present. Superficial reactions absent. Mentality normal. Nystagmus present.

Reiner, H.—1. Girl, aged 3 years. Involvement of upper (?) and lower extremities and trunk. Tendon reflexes absent. Electrical reactions: faradic diminished but prompt; galvanic diminished. Sensation normal. Superficial reactions present. Mentality normal. One of twins, the other dying intrapartum. Improvement was marked after two months.

2. Boy, aged 11 months. Onset at birth (?). Involvement of trunk and lower extremities. Tendon reflexes diminished. Electrical reactions: faradic and galvanic response both diminished. Sensation normal. Superficial reactions present. Hypermobility present.

Collier, J.—Boy, aged 5 years. Involvement of lower extremities. Tendon reflexes "difficult to obtain." Electrical reactions: faradic diminished. Hypermobility in ankles. Improved on rest and exercises.

Courtney, J. W., and Eaton, H. B.—Boy, aged 5½ years. Onset at birth. Quickening present. Speech defective. Drools. Involvement of trunk. Tendon reflexes absent. Electrical reactions: faradic normal (six weeks after first seen). Superficial reactions sluggish. Mentality normal. Circumference of head 53 cm. Patient was a 7-months premature baby. Improvement. After six weeks, knee-jerks and achilles jerks were present.

Dunn, C. H.—1. Boy, aged 5 months. Onset at birth. Quickening present but diminished. Face not involved. Involvement of upper and lower extremities, neck, and pectoral muscles. Tendon reflex absent. Electrical reactions not noted. Breathing abdominal. Died of bronchopneumonia.

2. Girl, aged 5 months. Onset at birth. Quickening present but faint. Involvement of muscles of deglutition, neck, and lower and upper extremities. Chest deformed. Involvement of muscles of shoulder girdle. Knee-jerks absent. Electrical reactions not noted. Died of bronchopneumonia.

Purser, F. C.—Boy, aged 2¼ years. Onset at birth. Quickening noted. Face not involved. Upper extremities and trunk, and especially lower extremities involved. Tendon reflexes absent, except that knee-jerks can be obtained at rare intervals. Electrical reactions: faradic diminished. Hypermobility. Sensation normal. Superficial reactions present. Nystagmus. Tremor. Mentality "average." Improved greatly.

Skoog, A. L.—1. Boy, aged 6 years. Onset at birth. Quickening absent. Involvement of muscles of face, neck, upper and lower extremities, and trunk. Tendon reflexes absent. Electrical reactions: response to faradic and galvanic current diminished. Hypermobility present. Sensation normal. Superficial reactions present. Wassermann negative. Spinal fluid negative. Mentality normal by the Binet tests. Improvement.

2. Brother of preceding. Boy, aged 4 years. Onset early in first year. Involvement of upper and lower extremities. Tendon reflexes negative. Wassermann negative. Spinal fluid negative. Mentality normal. Improved, regaining greater part of muscular activity. Muscle biopsy.

Strauch, A.—Girl, aged 3 months. Second child. Onset during second week. Action of facial muscles fairly strong but unless aroused, few facial movements are made. Nystagmus. Involvement of muscles of neck, arms, trunk, and legs. Respiration abdominal. Abdomen prominent and tympanitic. Constipated. All tendon reflexes absent except for a doubtful biceps jerk. Superficial reflexes absent. Electrical reactions: faradic absent; galvanic diminished but prompt. No sensory disturbance. Slight tendency to improvement during first month of observation, then stationary. Died of unknown cause at 5 months.

Sutherland, G. A.—Boy, aged 2 years. No involvement of face or trunk. Lower extremities involved. Knee-jerks absent. Electrical reactions not stated. Dilatation of colon with large fecal impaction. Foul stools. Hypermobility present. Mentality backward (?). Improvement in abdominal condition.

ABSTRACTS OF NECROPSIES

Spiller.—Aged 22 months. Muscles pale and flabby. Fibers small. Transverse striation well preserved; longitudinal not so distinct. Fatty infiltration and increase of connective tissue in which the nuclei are increased in number. No degeneration of the peripheral nerves, and the anterior and posterior roots are normal. Anterior horns normal, also the cord tracts and the cerebrum and cerebellum, with the exception of the paracentral lobules, in which the Betz cells are not normally numerous. Heart and thymus normal. Rigor mortis absent.

Baudouin.—Aged 4 months. Muscle fibers mostly small with some hypertrophied fibers. Anterior roots small (one-half normal size). Cells of the anterior horns small and probably reduced in number. Sclerosis of the thymus and of the thyroid.

Reyher and Helmholz.—Age not stated. No clinical details. Muscle fibers of various sizes, some thinner and some broader than normal. Transverse striations indistinct or absent and the longitudinal in some parts appear to be lost. Muscles infiltrated with fat and a very cellular connective tissue.

Collier and Holmes.—Aged 7 years. Muscles small and pale, except the diaphragm which is normal. A few hypertrophied fibers. Transverse striations distinct and the longitudinal "unduly" distinct. Great proliferation of the sarcolemma nuclei. Vacuolation of some fibers. Connective tissue and fat greatly increased. Peripheral nerves poorly myelinated. Anterior roots very slender; posterior normal. In the anterior horns the motor cells are only about one-third the normal number. Dorsal horns and Clarke's column normal. Thymus and thyroid normal.

Lereboullet and Baudouin.—Aged 15 months. Some muscle fibers small, some very large. Transverse striations have disappeared, but the longitudinal are distinct. Great proliferation of the sarcolemma nuclei. Connective tissue increased. Anterior and posterior roots normal. No diminution in volume and no degeneration in the anterior horns. The brain is normal. Thymus, thyroid, and adrenals normal.

Rothmann.—Aged 5 months. (Case reported clinically by Haberman.) Muscles pale. Size of fibers not noted. Many have disappeared. Transverse striations distinct. Marked increase of the fatty tissue and connective tissue, the latter rather cellular. No degeneration in the peripheral nerves, but a marked increase in the connective tissue; nerve fibers small, but with a distinct medullary sheath. Anterior roots small and a large proportion of the fibers lack medullary sheaths. Posterior roots normal except in the lumbar region where they are atrophic. In anterior horns, cells very much diminished in number and the large ganglion cells absent. In the dorsal segments the posterior cells also fewer than normal. The large cells also absent in Clarke's column, and minor changes in the anterolateral tracts. The hypoglossus nucleus also shows a diminution in the number of cells and chromatolysis is noted in those present. No degeneration in the cord or the spinal roots. A notable feature of this necropsy is the examination of the nerve-endings in the muscles. It was found that the entrance of the nerves into the muscle fibers could be seen but that the end-plates were absent. In the cord, the glia is increased, as apparently is the number of vessels, the latter having thickened walls without intimal changes. Some perivascular hemorrhages in the cord. Cerebellum small. Heart normal. Thymus very large, with thickening of the walls of the vessels. Rigor mortis absent.

Pollak.—The details of this necropsy have never been published. Thymus larger than normal. Thyroid large.

Archangelsky and Abrikosoff.—Aged 7 months. Muscles pale and flabby excepting the diaphragm and the muscles of tongue and pharynx. Fibers very

small; some hypertrophied fibers. Transverse and longitudinal striations distinct. No increase of sarcolemma nuclei, fat or connective tissue. Cohnheim's fields normal. Nerve endings normal. In the peripheral nerves one-third to one-half of the fibers are not myelinated. No degeneration. The anterior roots are only about one-fourth the size of the posterior, and only about one-half of the fibers are myelinated. Posterior roots and their fibers normal. Cells of anterior horns very few and small; those in the posterior horn larger. Some slight changes in the staining properties of Gower's and the pyramidal tracts without evidence of degeneration. No change in the neuroglia. In the cord many fibers are not myelinated, and even those which are, seem to be smaller than normal. Rigor mortis absent. Embryonal fatty tissue present around the kidneys. Nerve-endings in muscles present (no statement as to end plates).

Berghinz.—(No clinical details. Doubtful case.) Cells of anterior horns small and few. Nerve cells of cerebellum small. Hypoplasia and microgyria of the cerebrum. Glands of internal secretion normal.

Councilman and Dunn.—Aged 7½ months. Muscles small, flabby, grayish and translucent, excepting the diaphragm, which is normal. Many of the fibers small, the larger ones being of normal size. Transverse and longitudinal striations present in most fibers, but absent in some. No actual increase in sarcolemma nuclei, but these appear numerous because of the small size of the muscle fibers. No fatty degeneration. In the affected muscles the peripheral nerves lack myelin and some are degenerated. The fibers in the roots of the cord are normal. There is no apparent reduction in number of the cells of the gray matter in the cord. Neuroglia normal. No nerve-endings are found in the affected muscles. Heart, blood vessels and adrenals normal. Thymus large (29.2 gm.). Thyroid small. Rigor mortis absent.

Griffith and Spiller.—Aged 25 months. Muscles pale, soft, flabby. Most muscle fibers small; a few hypertrophic. Transverse striations distinct; longitudinal not distinct. Sarcolemma nuclei "excessive" in number. Some muscle fibers are vacuolated and give the reaction for fat. Connective tissue increased. Marked degeneration in the posterior tibial nerve, not in the median. Anterior roots small, with degeneration in the seventh and eighth cervical. Posterior roots normal. The cells of the anterior horns very few and small. Clarke's column normal. Brain very large (1,542 gm.). Pia of the cord edematous. Blood vessels normal except in the calf muscles, where they are much sclerosed. Heart pale, yellowish gray, and of good consistency, but the papillary muscles are pale and short. Heart muscle shows distinct cross striation, but there is a good deal of polar pigment. Thymus small. Thyroid small. Adrenals small, pale, yellowish, and show absence of chromaffinic cells.

Mensi.—(Five cases reported together.) Ages 1 day to 1½ months. Muscle fibers and bundles slender. Cross striations absent or indistinct. No nerve-endings can be found. Anterior horn cells reduced in number and are prevailingly multipolar, with the large ganglion cells absent.

Marburg.—Aged 3 months. Fibers in part very small and in part of larger—probably normal—size. Transverse striation present except in the very smallest; longitudinal also distinct. Sarcolemma nuclei only apparently increased by contrast with the smallness of the muscle fibers. Replacement of the muscle by fat and connective tissue. In peripheral nerves no degeneration but fewer fibers than normal and these deficient in myelin; connective tissue increase. Deficient myelinization of the anterior roots; posterior roots normal. The cells of the anterior horns are few, small, and pyknotic. Cells of posterior horns and of Clarke's column normal. Fibers of the cord tracts deficient in myelin. There is a connective tissue and neuroglia increase in the cord and the vessels have thickened walls. Thymus, thyroid and adrenals normal.

Concetti.—Aged 53 days. Muscles soft and pale. Muscle fibers: some small, some normal, some hypertrophic. Transverse and longitudinal striations nor-

mal. Sarcolemma nuclei not increased. No increase of connective tissue. No hyaloid fibers. In the peripheral nerves a few fibers lack myelin but there is no degeneration. The anterior roots are a little smaller than normal. Anterior horn cells very few and very small. Large ganglion cells absent. Cells fusiform and pyknotic. Clarke's column and the pyramidal tracts normal. In the cerebellum the Purkinje cells are few and altered in shape. All layers of the cerebrum reduced in volume. Glia normal.

Foot.—Aged 3½ months. Muscles pale, resembling raw pork. Muscle fibers: some very small, some moderately small, some normal. Transverse and longitudinal striations present. Sarcolemma nuclei not increased. Connective tissue not increased. Fatty changes in some fibers and some fibers are hyaloid. Some areas of round cell infiltration in the rectus abdominis. The peripheral nerves show very defective myelinization. Cells of the anterior horns reduced in number and size. Some are vacuolated and many are misshapen. The tracts, excepting the posterior and the direct cerebellar, are pale, showing deficient myelinization. Normal nerve endings in normal fibers, but none in the small fibers. Marked gliosis in the anterior horns. Cerebrum normal. Heart, thymus, thyroid and adrenals normal.

Kaumheimer.—Aged 4 months. Muscles pale and thin. Many small muscle fibers and some hypertrophic. Transverse striations distinct except in hypertrophied fibers. The fibers contain abundant nuclei. Increase in the fat and connective tissue. In the peripheral nerves, the number of fibers is diminished and there is an increase in the connective tissue, but no axis cylinders without medullary sheaths are found. Schwann's nuclei increased. Anterior roots small. Cells of anterior horns few, small, misshapen and pyknotic; in some places only cell shadows remain. In tracts some degenerated fibers but none deficient in myelin. Cells in Clarke's column show changes similar to those in the anterior horns, as do those in the hypoglossus nucleus which appear to be severely involved. Patchy gliosis in the cord, and some large "neurophage" cells. No evidence of an inflammatory process. Rigor mortis absent except in the lower jaw.

Strauch.—Aged 3 months. (Muscle only examined.) Muscle pinkish. Fibers small, of various sizes. No hypertrophic fibers. Transverse striations less distinct than normal; longitudinal indistinct. Enormous increase of sarcolemma nuclei with mitotic figures, indicating regeneration. One third to one half of the muscle consists of areolar tissue. The nerves in the muscle are slightly deficient in myelin and show an increase of the connective tissue.

MUSCLE BIOPSIES

Bing.—Aged 3½ years. No abnormalities except an increase in nuclei.

Collier and Holmes.—Aged 3½ years. Muscles pale, fatty, with little muscle tissue visible. Fibers very small excepting many hypertrophic fibers. Transverse striations distinct, also longitudinal. Great proliferation of the sarcolemma nuclei. Connective tissue increased. Nerve fibers poorly myelinated. Thickening of vessel walls due to a periarteritis with foci of small cells at intervals. Some intimal proliferation.

Openshaw.—Aged 7½ years. Hamstrings tough and fibrous. Vastus internus anemic and yellowish. Transverse striations absent. Fatty infiltration and "signs of regeneration" are noted.

Skoog.—Aged 22 months. Muscle pale. Fibers small, none hypertrophied. Transverse striations lost. Sarcolemma nuclei four to five times as numerous as normal. Increase of fat and connective tissue. Vessel walls show great thickening of the adventitia. Intima not involved.

Skoog.—Aged 6 years. Triceps and quadriceps examined. All fibers small, none hypertrophied. Fibers hyaline in appearance. Transverse striations absent in most fibers. Sarcolemma nuclei somewhat increased. Fat and connective tissue increased. Some "arterial capillaries" have thickened walls. Arteries normal.

Biopsy on the 4-year-old brother of this patient showed the same changes.

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THE EPIDEMIOLOGY OF BACILLARY DYSENTERY*

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BOSTON

Bacillary dysentery takes a heavy toll of the infants of large cities every summer. The disease is not spectacular, for it usually does not spread over large areas, but strikes at random here and there and passes by almost unnoticed. During a period of ten years, however, the case incidence is probably higher than the greatly feared poliomyelitis, and the death rate is equally high.

The cause of the disease is well recognized, and its treatment has received careful study, but the mode of transmission has excited only indifference, or, at most, random speculation. Epidemics of adult dysentery have received much attention, particularly during the present war, for the disease has at times wrought havoc among the soldiers. The source and the mode of transmission of the casual case, the sporadic case, the usual type of summer bacillary dysentery of infants is unknown. Kendall[1] believes that the disease in infants is spread by the factors which cause other intestinal infections and emphasizes the importance of contact with carriers. Zinsser[2] has described a small milk epidemic in children, and Amoss and Lucas[3] have established the menace of fly transmission. The Floating Hospital has felt that the most important step in preventing the constant stream of cases of bacillary dysentery that flows to its wards every summer was to undertake the study of the mode of transmission of the disease and the source of infection of the infants.

There are several inherent factors which were most favorable to such a study. The victims were infants, usually under 18 months of age, and therefore their activities were limited; they travel but little, come in contact with few people, and eat only one, or at most but a few articles of food. In fact, we soon found that it was comparatively easy to trace the infection of a baby under 1 year, though much more difficult after the child was old enough to walk, for then they run up and down the street, come in contact with other children, and eat whatever they pick up.

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1. Kendall: Boston Med. and Surg. Jour., 1913, **69,** 741.
2. Zinsser: Proc. New York Path. Soc., 1907, p. 162.
3. Lucas and Amos: Jour. Exper. Med., 1911, **13,** 486.

Another advantage of the study was that the diagnosis of bacillary dysentery is clear cut; with, first, a definite clinical story; second, by means of the isolation of the dysentery bacillus from the stools, and third, the development of specific agglutinin in the blood. It is true that the clinical picture is not always definite, the isolation of the bacillus from the stools is difficult, and the agglutinins develop slowly — in ten to twelve days — and in the mild cases may not appear at all.[4] In this study, no case is reported as positive without showing at least two of the three positive factors.

There are certain well-established facts about the disease which furnish a good working basis.

1. The disease is due to the dysentery bacillus, which has been well described and is readily recognizable.

2. The dysentery bacillus is found in the feces only and not in the other excretions, as in typhoid fever. Thus every case must represent some short path between the infected feces and the mouth of the victim.

3. The incubation period of bacillary dysentery, in adult cases, at least, is short — from three to seven days.

4. The disease in infants is in most instances a summer disease, with highest incidence in July, August, and September.

5. Bacillary dysentery is more common in children of poor parents.

There are certain assumptions that have been believed to play an important part in summer bacillary dysentery of infants.

1. The case incidence of bacillary dysentery bears a close relation to high temperature and high relative humidity.

2. Bacillary dysentery is most common in dirty, unhygienic homes, flourishing among the tenements.

3. Bacillary dysentery is particularly prevalent among the infants of foreigners.

With these facts and assumptions, we had a foundation on which we began to build, adding a few stones to the structure, and tearing down here and there a loose fragment. The investigation included: First, a study of the community conditions and factors affecting every individual. A daily record was kept of the maximum, minimum, and mean temperatures, and of the relative humidity and barometric pressure throughout the summer, in order to show the relation between these factors and the case incidence of bacillary dysentery. Second, beside community conditions, a record of neighborhood conditions was kept. A daily report was received from the boards of health of the city of Boston and all of the neighboring cities, and from the State Board of Health, of all reported cases of bacillary dysentery, in order

4. Villard and Dopter: Ann. de l'Inst. Pasteur, 1903, **17,** 463.

Chart 1.—Spot map of bacillary dysentery of infants in Boston and vicinity during the summers of 1915 and 1916. Each black dot represents a case of dysentery. The nests of infection in certain portions of the South End, A, and in South Boston, B, are striking. Sanitary conditions are equally bad in the North End, C, and West End, D, but the former neighborhoods are occupied largely by first generation Irish-Americans, and the latter by foreigners—Italians, Poles, and Russian Jews. Most factors affecting the health of infants in both neighborhoods are the same, the same water, the same milk supply, the same temperature and humidity, and equal number of flies, etc. The only factor that is not common to both neighborhoods is food, for most foreign mothers nurse their babies, while many American mothers do not.

to expose nests of infection in various parts of the city and state. A spot map was kept of all cases to show the infection centers. Third, the housing conditions of each case were studied, and a score card system of recording the conditions in each home was devised. The nationality of the parents was recorded. Finally, a careful investigation was made of the activities of each infected baby for a period of ten days before symptoms developed. This investigation included food eaten, contact with individuals, places visited, and the history of any illness in the house or neighborhood.

The investigation was begun in each instance from a definite point, a proved case of bacillary dysentery by means of the isolation of the bacillus from the stools. This meant a delay of three to four days, which, together with the three to four days from the beginning of symptoms until entrance into the hospital, made an interval of a week between the onset of symptoms and the beginning of the epidemiologic work. This delay was a serious handicap to the study, but was compensated for by the great advantage of dealing only with proved cases of the disease.

We are able to report the study of seventy-five cases in all, forty-nine of them being hospital cases, while twenty-six cases were discovered in the course of the investigation. The first case developed June 15. The last case studied developed September 1. There was a continuation of the disease after September 1, but the hospital closed September 15, so no more stool diagnoses could be made, and automatically the work stopped.

It is obvious that seventy-five cases are not a sufficient number from which to draw conclusions as to the effect of temperature and humidity on the case incidence of bacillary dysentery. Grover[5] has reported the statistics of several thousand cases of diarrhea in Greater Boston and believes there is close relation between diarrhea of infants and a high humidity and temperature, but so far as our brief studies go, there seemed to be no relation between high temperature and humidity and dysentery. There was one period of severely hot weather, with a corresponding increase in the number of hospital admissions and of infant deaths in the city, but there was no increase in bacillary dysentery. The case incidence is more closely related to the incidence of flies, for the disease had hardly begun before the hot weather was over, and the cases lasted well into September and long after the humid weather was past, though flies were still in abundance.

The disease was not more common in children of foreigners. The most ignorant and destitute foreigners in Boston are the Poles, though the Italians and Russian Jews in certain quarters are living under

5. Grover: Jour. Am. Med. Assn., 1916, **67,** 1562.

almost as unfavorable conditions. One would expect, therefore, a high case incidence among these people, but on the contrary, the families chiefly affected were not the illiterate foreigners, but the careless and neglectful poorer class American families, or more particularly the first generation families. A summary of the parentage in the cases is interesting:

American, including Canadian	33	Polish	2
American-Irish, first generation	17	French Canadian	2
American-Italian, first generation	4	Negro	1
Irish	4	Greek	1
Italian	4	Unclassified	4
Jewish	3	Total	75

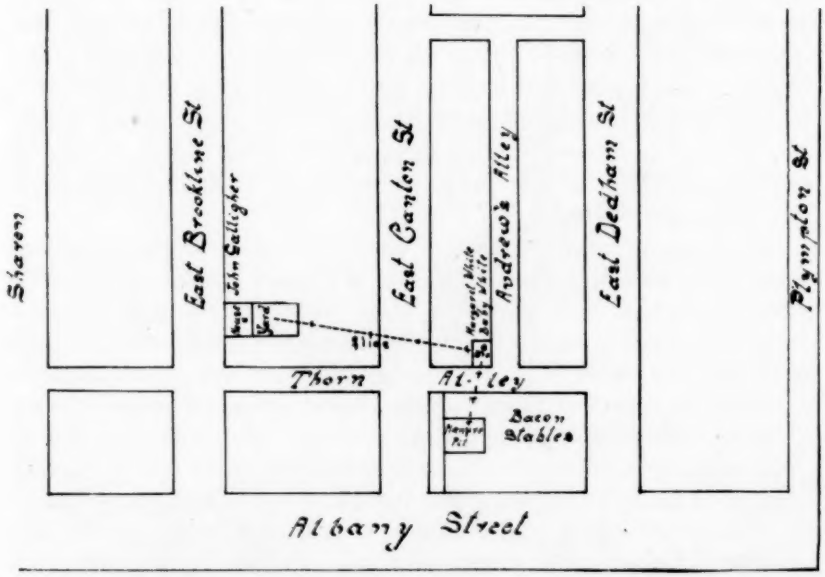

Chart 2.—Diagram illustrating the method of introduction of bacillary dysentery in a community in the early summer, and its mode of transmission. The W. family lived in a miserable unscreened tenement in Thorn Alley. The oldest sister had dysentery in the summer of 1915 and was a carrier. June 26 the younger sister developed dysentery, and since the stools were not disinfected, and flies swarmed into the sick room from a stable across the alley, it is not surprising that the baby brother developed dysentery June 30. J. G., living 150 feet away, also developed dysentery. The two families had nothing in common, but J. G. played in the back yard and was probably infected from the W. family by means of flies.

I do not attribute this surprising situation to the greater uncleanliness or worse sanitary conditions of the American homes, for quite the contrary is the case. It is due to the simple fact that most foreigners nurse their infants, while American mothers often do not. It is interesting to note in this connection that but one of our cases of

bacillary dysentery was a nursing baby, and this child was nursed only at night and was fed condensed milk during the day.

Though squalor, poverty, and filth go hand in hand with bacillary dysentery, they are not necessary accompaniments of it, for the disease may be found in the better homes in the better portions of the city and may be entirely absent in the most unsanitary portion of the city. For example, Boston's West End tenement district had almost no cases in the summer of 1916, and the North End very few, though unsanitary conditions are fully as bad in either of these localities as in the South End, where the disease abounded. Young[6] studied the geographic distribution of the Floating Hospital cases in 1910 and found a somewhat similar localization of cases. In 1915 there was a nest of cases in the South End, with twenty or more cases within a radius of only one-eighth of a mile, while in 1916 there were a few scattering cases within this nest, but another nest of cases was found directly across the river in the tenement district of South Boston (Chart 1). Unsanitary conditions, therefore, do not cause dysentery, but they are a fertile soil, needing only the introduction of the seed in order to produce a widespread harvest of cases.

To show the relation between bacillary dysentery and unsanitary household conditions, a housing chart was made of the homes of the infants, based on the score card system, similar to the dairy or market score cards, with a total of 100 points for ideal conditions. Records were kept, for example, of the number of rooms per person, allowing 5 points for a perfect score; of the number of windows per person, 5 points; screening, 5 points; ventilation of living-room, 2 points; of sleeping-room, 3 points; cleanliness and neatness of the house, 5 points; location of the toilet, if clean, well ventilated, and convenient, 5 points; provision for the care of the diapers, if protected from flies, 2 points, if boiled, 3 points. If pasteurized milk was used, 10 points were allowed, and the intelligence of the mother was graded for 10 points.

Forty-one homes were scored, the highest score being 94 per cent., the lowest, 15 per cent., the average 59 per cent. The average housing score in those cases of dysentery due to direct contact, however, was only 48 per cent., and the average housing score of those that were a source of infection to others was 41 per cent. This is but a complicated way of saying that a child is more likely to contract bacillary dysentery if it lives in a dirty, unhygienic house and has a careless and ignorant mother, and a baby with dysentery in a dirty, unhygienic home is most likely to be a source of infection to other children.

The study of the source of infection in the various cases was in the nature of a general survey rather than an intensive investigation.

6. Young: Boston Med. and Surg. Jour., 1911, **164,** 299.

The activities of the infected child were studied for ten days before symptoms began, and a careful, detailed record was made of every place the child had been, of all contact with individuals, of all food eaten, or of any factor that might be a source of infection to the child.

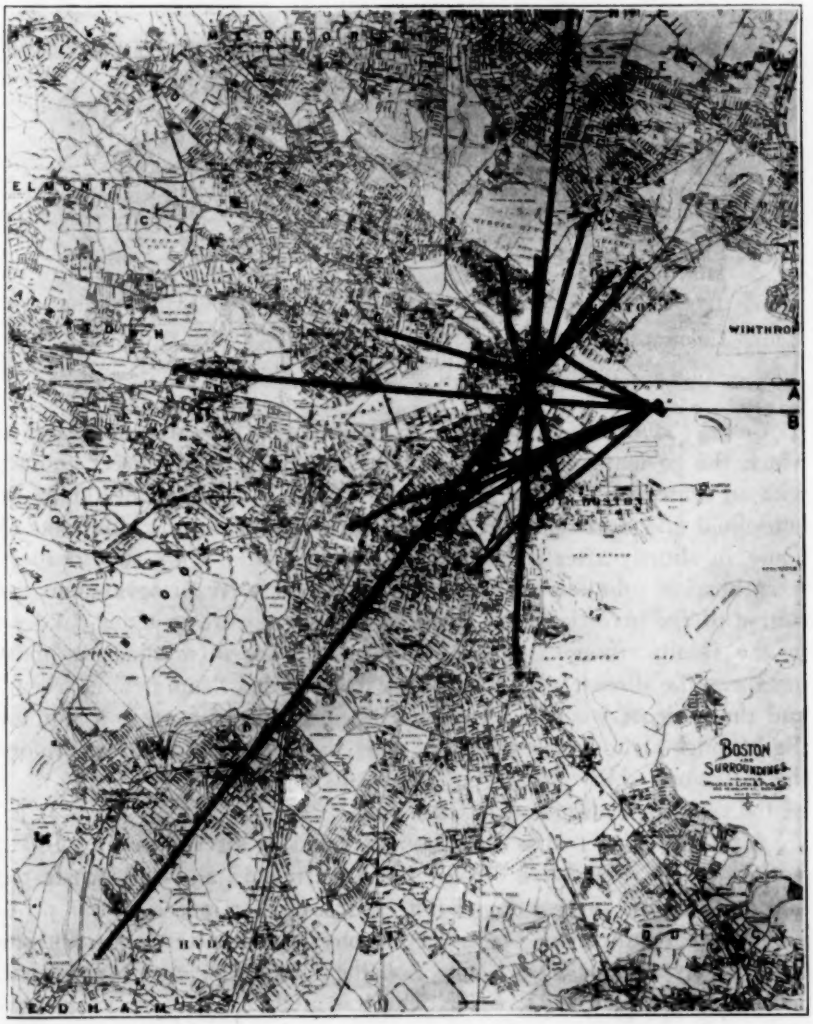

Chart 3.—Map of Boston and vicinity illustrating the epidemiology of widely scattered and isolated cases of bacillary dysentery. Thus, there were fifteen cases in various parts of the city, some of them in isolated suburbs. The only factor in common was S. brand of condensed milk. A. Nine cases were due to the use of icecream cones. B. Twenty-seven cases were due to direct contact. Thus, though we studied seventy-five cases, the foci of infection of these cases were reduced to twenty-eight, and no doubt more intensive study of the cases from unknown sources would have reduced the number of separate foci of infection still more.

A summary of the probable source of infection of the cases is as follows:

Total cases	75
House cases	49
Discovered cases	26, of which 18 were children 8 adults
Average age of hospital case	1 to 2 years
Average age of discovered case	4 to 8 years (other than adults)

Etiology of the seventy-five cases is divided as follows:

	Cases
Contact with an acute case	21
Contact with a carrier	2
Contact with house cases	4
Condensed milk epidemic	15
Icecream "cones"	9
Flies	6
Milk	1
Water	1
Fruit	1
Unknown	15
Total	75

Contact with an Acute Case. — There were twenty-one cases in which the patients developed bacillary dysentery from direct contact with an acute case. These patients were usually of the same family or household and developed the disease during the time the child was at home, or shortly after it was sent to the hospital. Only two of these were hospital admissions, while the remainder were discovered in the course of the investigation. Most of the cases were in older children in the family, though eight of the cases were in adults. In most instances the disease was so mild as to be called "summer diarrhea," and the patients would seldom have seen a physician were it not for the hospital visitor. As a general rule, the older the child, the milder the infection, while only two of the adults were seriously ill, and none of the twenty-one contact patients died.

A typical contact infection was illustrated by the H. family. G. H., 3 years of age, developed bloody diarrhea June 15 and was prostrated and quite ill for several days. The source of her infection was probably an icecream cone. There was no physician in attendance, and the child received poor care. The housing conditions were very poor, scoring only 49 per cent.; a dirty, careless mother, and a dirty, slovenly house. June 19, the mother developed severe abdominal cramps and diarrhea. She took "patent" medicine and was never confined to her bed, though she had "some fever." June 21, Lillian, a daughter 12 years of age, developed diarrhea, but no blood was noted in her stools. She had no physician and was in bed only one or two days. Finally, June 29, Francis, the baby, 8 months of age, developed a severe bloody diarrhea and was brought to the Floating Hospital. The dysentery

bacillus of the Flexner type was isolated from his stools and our investigation begun. The blood from the other three members of the family agglutinated the bacillus isolated from the baby's stool in dilutions up to 1 to 300, and also agglutinated other strains of the Flexner type in lesser dilution — up to 1 to 160.

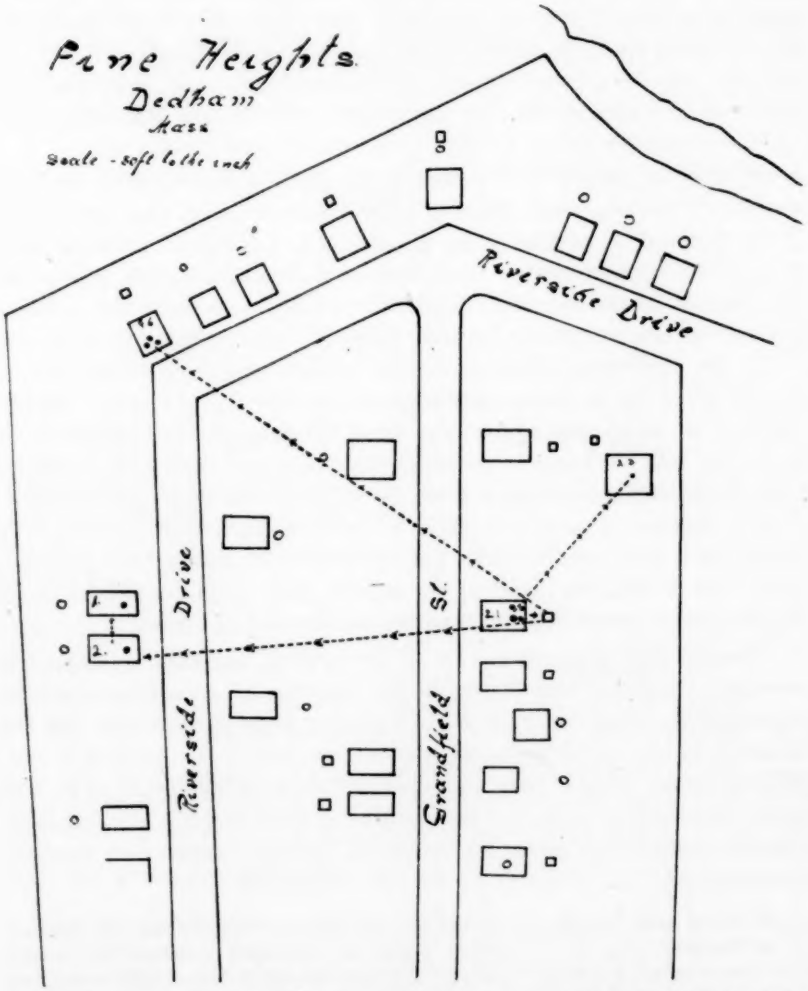

Chart 4.—Diagram illustrating the mode of transmission of the Shiga infection in Pine Heights. L. C. returned from the Haverhill Fresh Air Farm with severe bacillary dysentery and remained in the community three days (House 21). By direct contact she infected two sisters and a brother. A voluntary nurse carried the infection home to her husband (House 23). The infected feces were thrown into an open privy, and flies carried the infection to House 86 and House 2. Raymond G. in House 1 was infected by direct contact from House 2, and from the case of R. G. the investigation began.

Other examples of contact infection with an acute case might be given, but the one instance illustrates the points, and other examples will be mentioned in subsequent paragraphs. The important facts are that many of these contact cases were in older members of the family, and in these persons the course of the disease was mild, so mild that it was commonly called a simple "summer diarrhea." Undoubtedly many cases of summer "ptomain poisoning" are really mild bacillary dysentery. These sporadic cases are seldom serious in themselves, but the patients may be a great menace to the community, particularly to the babies of the community, for our studies have shown that mild adult cases may readily infect a baby, with rapidly fatal results.

It may be stated as a general rule that in every dirty, careless household visited, where the sick child remained more than one week, there resulted a contact case of bacillary dysentery. There were twenty-one contact cases, from forty-nine house cases, all proved by the isolation of the dysentery bacillus from the stools or by the development of specific agglutinins in their blood. There were other suspected cases, but agglutinins develop slowly, seldom appearing before ten to twelve days, and in mild cases they may not develop at all. No case is reported in which the agglutinins were not present in dilutions of at least 1 to 160. Whenever possible, the strain was used for agglutination which had been isolated from the stool of the corresponding case. In this manner, a greater number of contact cases were proved than would have been possible with the use of a stock strain for agglutinations. As a rule, the blood of the milder cases agglutinated the stock strains, but in lesser dilution than the corresponding strain.

Contact with a Carrier.—In all probability, bacillary dysentery is introduced into the community in the summer by a carrier, and once begun, other factors carry it on. We know there are carriers, but the isolation of the dysentery bacillus from the stool of a carrier is a very difficult thing. I have only two cases to report which seem to be due to contact with a carrier, both cases occurring early in the summer. The W. family is a good illustration of the introduction of bacillary dysentery into a community in the early summer.

M. W., 5 years of age, developed bloody diarrhea June 26 and was brought to the hospital July 2. The Hiss Y-type of dysentery bacillus was isolated from her stools. An investigation showed no illness in the neighborhood and none in the household. The food was not suspected. Her older sister, 15 years of age, had had a severe diarrhea ten months before, lasting about ten days but had no medical attention. We made repeated examinations of this older child's stool but failed to find the dysentery bacillus, though her blood readily agglutinated the strain of dysentery bacilli isolated from her sister's stool in dilution of 1 to 100.

The sanitary conditions of this home were very bad, the housing score being only 15 per cent. M.'s stools were not disposed of for hours at a time and were exposed to flies which swarmed in from a nearby stable.

June 30, Baby W., 3 months of age, developed a moderate, greenish, slimy diarrhea, without blood. Nevertheless, he was sent to the Floating Hospital, and dysentery bacilli were isolated from his stools. July 5, the report came from the city board of health of a case of bacillary dysentery within 150 feet of the W. family, and investigation proved the case to be of the same type as the W. infection. This child, 2 years of age, lived in a clean, sanitary home, under ideal conditions, with a housing score of 86 per cent. He had not been away from home or in contact with other children, and all his food was well cooked. The child commonly played in the back yard, on the side toward the W. family tenement. Since flies were so prevalent in the W. household, since they had ready access to infected diapers, since there were no other cases of bacillary dysentery in that part of the city, the only connecting link between the cases would seem to be the flies (Chart 2).

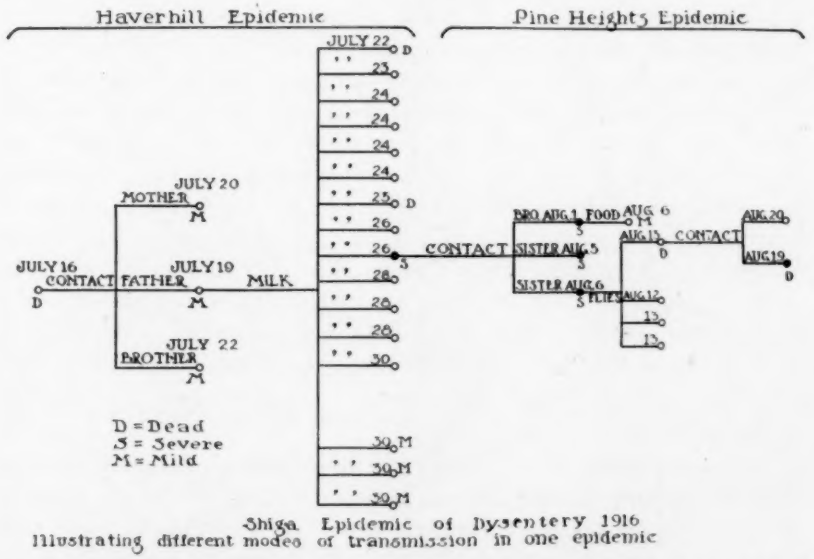

Chart 5.—Diagram illustrating the various modes of transmission of bacillary dysentery in several communities during a single summer. The first infection was from icecream in Lawrence and was transmitted by direct contact to a dairy worker in Haverhill. The dairy worker infected the milk, which infected a large number of children in a fresh air home. One of these children returned to her home in Pine Heights and spread the infection by contact, by flies, and an intermediary carrier.

Another possible contact with a carrier case was R. S., 10 months of age, whose illness began June 30. There were no other cases in that part of the city, the child had not been away from home, and his only food was milk, which was pasteurized. Just one year previously, his sister had been a patient in the Floating Hospital with bacillary dysentery. The same type of bacillus had been isolated from her stools as was obtained from the baby brother's stool. At the time of the investigation, the older child was in perfect health, and repeated examinations of her stools were made for dysentery bacilli, with negative results. The father gave a history of bacillary dysentery during the Spanish-American war. Examination of his stools was also negative, and neither the father's nor sister's blood agglutinated the strain isolated from the baby's stool. Despite these negative findings, it seems probable that either the

sister or father was a carrier and infected the baby. This conclusion is open to question because of the difficulty of detecting dysentery carriers. The rest of the story is almost exactly that of the W. infection. After a proper incubation period, the city board of health reported three cases of bacillary dysentery within 100 yards of the L. tenement. In this family, the mother and 3-year-old sister were infected by direct contact with a baby brother. This baby was probably infected from the L. baby by means of fly transmission. These conclusions were reached because flies were abundant and had ready access to the infected stools, there were no other cases of dysentery in the neighborhood, the child had not been away from home, its food was thoroughly cooked, and other sources of infection were excluded.

Hospital Contacts.—Four babies developed bacillary dysentery in the wards of the hospital. Each child was admitted with quite a different diagnosis, and their stools were negative on entrance. Each developed the disease seven to ten days after admission, and in no instance did the child come from an infected home or neighborhood.

This is not a criticism of the hospital staff, but I simply mention these four cases to illustrate the remarkably contagious nature of the disease. In the homes, twenty-one cases were spread by contact with an acute case, and as a rule the infected baby remained in the home less than a week, while but four contact cases developed on the wards, though there were virulent cases on the boat all summer.

It is important to emphasize that extraordinary precautions must be taken to prevent ward infection, and no hospital has a right to admit cases of bacillary dysentery unless it has the facilities for their isolation, for rigid "enteric precautions," and particularly for absolute fly exclusion.

The Condensed Milk Epidemic.—About July 15, patients began to come to the hospital who gave a history of using one of the cheaper brands of a large producer's condensed milk. By August 15 there were fifteen cases from all parts of the city with a clear-cut history of using the S. brand of condensed milk. The epidemic ceased as abruptly as it began.

CASE 1.—A baby, 8 months of age, became ill July 8. The child had been fed on S. brand condensed milk for three months. July 5 the mother bought a fresh can, and three days later the child became very ill and was brought to the hospital, where a diagnosis of bacillary dysentery was made. The child had eaten nothing but S. brand condensed milk and boiled water, had not been away from home, and there was no sickness in the neighborhood. A sample from this can was obtained July 13, but no dysentery bacilli were found.

CASE 2.—Baby 5 months old developed bacillary dysentery July 14, came to the hospital July 26, and died soon after. The baby had eaten nothing but S. brand condensed milk for three months, had not been away from home, and there were no cases in the neighborhood. Other members of the family, mother, father, and two children, aged 9 and 7, used the same milk, but only in tea or coffee. One child, 2 years of age, used the condensed milk diluted with water. The 2-year-old child developed bacillary dysentery July 24, whether from the milk or from contact with the baby is not known. The father developed bacillary dysentery July 27, the disease running a mild course.

CASE 3.—Baby boy 7 months old, became ill July 17 and was brought to the hospital, where the diagnosis was made. The family lived in an isolated suburb, and the baby was not in contact with other children. The mother was a trained nurse and was intelligent and very cleanly. She carefully boiled the baby's water, then cooled it and added S. brand condensed milk. This was the only food the child had.

CASES 5, 6, 7, 8, 9.—The F. family consisted of mother, father, and four children, aged 4, 3, and 2 years, and the baby of 10 months. The father was a fisherman and was out at sea. August 2, the baby was brought to the hospital with severe bacillary dysentery. The child had been fed on nothing but S. brand condensed milk and boiled water for three months. The mother obtained a fresh can July 24. July 26, the mother and all four children developed a prostrating diarrhea. All recovered in two to five days except the baby. The only food used in common by all was S. brand condensed milk. The only food the baby had had was condensed milk, but the older children had been given bread, butter, eggs, and cooked vegetables, though they had had no icecream, fruit, nor fresh milk. There was but one case of sickness in the neighborhood, a child of 2 years, reported by the city Board of Health as bacillary dysentery. This child's mother had bought a can of the same milk from the same store at about the same time as the F.'s did, and her baby became ill July 23. The parents were noncommunicative and would not permit taking blood for agglutinins, though the history was typical.

Blood was obtained from all the F.'s, however, and all agglutinated the strain isolated from their baby's stool in dilutions of 1 to 160 or higher.

CASE 10.—Mary R., a baby 6 months old, became ill August 3. The mother customarily heated the water to boiling and then added S. brand condensed milk. During the week of July 27 the mother went to work, leaving the baby with a 12-year-old sister. The amateur nurse mixed the S. brand condensed milk with cold water and gave the mixture to the baby without warming it at all. One week after the baby became ill, a 2-year-old sister developed bacillary dysentery, but no physician was called. When seen by the hospital visitor, the 2-year-old child was well, but her blood showed agglutinins in a dilution of 1 to 160 for the strain isolated from her baby sister's stool. This child may have been infected by contact with her baby sister or from the condensed milk. One week later, a cousin 7 years of age developed a moderately severe diarrhea. He had playd with his cousin during her convalescence and was probably a contact case. His blood also showed agglutinins in dilution of 1 to 160.

CASE 11.—Another mother reported that she had not used S. brand condensed milk in the child's food for a month, having substituted a pasteurized milk formula. Later she admitted that the new mixture had not been sweet enough to suit the baby's palate, and though she carefully sterilized the food, she afterward added one-half teaspoonful of S. brand condensed milk to each feeding.

CASE 12.—In one instance, a child of 18 months lived in a suburb under excellent home conditions and was given only pateurized milk. On two mornings, however, the milk delivery was late, and the mother gave the baby a feeding of S. brand of condensed milk. Four days later the baby developed bacillary dysentery.

The finding of dysentery bacilli in the milk is the only evidence lacking to prove that the epidemic was due to S. brand of condensed milk, and without this evidence my case collapses. Stock samples of milk were repeatedly examined, with negative results, and in two instances I was able to obtain the can from which the infection was

supposed to have come seven to ten days before. Both samples failed to show dysentery bacilli.

Nevertheless, the evidence is very suggestive. Fifteen cases of dysentery of the same type, from all parts of the city, some of them in isolated communities, developed about the same time, and with but one factor in common, the use of S. brand condensed milk, and in most instances it was the only food of the infected child. None of the hospital admissions for dysentery before July 10 or after August 15 used this brand of condensed milk.

For these reasons, it seems most probable that one portion of one shipment of one brand of condensed milk, delivered about July 10, was infected with dysentery bacilli.

Flies.—Indirectly, flies have already been mentioned as a means of spreading bacillary dysentery. It is a difficult thing to prove anything on a fly. Alice Hamilton[7] found typhoid bacilli on the bodies of flies caught outside a typhoid patient's windows, and Amoss and Lucas[3] caught flies "red-handed" with dysentery bacilli on their bodies.

I believe that seven of our cases are due to infection through the medium of flies, but the evidence is circumstantial only. Several instances of fly transmission have been mentioned in connection with other outbreaks. A typical example of fly transmission may be given.

T. C., 9 months of age, came to the Floating Hospital, August 17, with severe bacillary dysentery. The source of his infection was never discovered. He was taken home against advice August 25, though he was very ill, passing fifteen to twenty bloody stools a day. Ten days later, a baby 3 months old, living just around the corner, developed bacillary dysentery, came to the Floating Hospital, and died. The strain isolated from the stools of both babies were the same type. The two families did not know each other and had nothing in common. The second baby had not been away from home and had been given only pasteurized milk. The back doors of the two families were less than 50 feet apart, and the diapers of the first child were kept on the roof or in an open room for hours without cleansing or disinfection. Flies were in abundance, and neither house was screened. There is no direct proof that flies did carry the infection across that 50 feet from one house to another, but the circumstantial evidence is strongly against the fly.

The other six cases that I have classified as due to fly transmission are almost a repetition of this story. The tenement mother is too ignorant, or many times too careless to protect her baby's stools from flies, and the diapers are seldom boiled. Since flies are so abundant in the tenements, and screens are almost never seen, it is most extraordinary that more cases are not carried in this way. It is more than probable that some of the fifteen cases from unknown sources are due to flies, but as we said at first, it is hard to indict a fly.

7. Hamilton: Jour. Am. Med. Assn., 1903, **40,** 576.

Icecream.—It is a curious thing that a city which is so careful about its milk supply and other foods should practically neglect a food that is almost as universally consumed, in the summer, at least, as milk itself. Icecream "cones" are the presumable source of infection in nine of our cases. The evidence is not absolute, for most of the children were older than in the other types of infection — between nine months and four years — and their activities were more varied. They played in the streets, ate various articles of food, and came in contact with many children, and thus their epidemiology is much more indefinite than that of infants.

In each case attributed to icecream, the infection came through the one cent icecream "horn" sold in the filthy basement confectionery shops. In each instance, the criteria were that the child had not been away from home, had not been in contact with sick children, there were no other cases of dysentery in the neighborhood, other food eaten was beyond suspicion, and the icecream was eaten within six days.

A good example is the Jack Frost Ice Cream Company's cones.

R. K., 15 months old, lived in a splendid home in a suburb. There were no cases of dysentery for miles, and the child had not been away from home. July 30 she was given an icecream "horn" of the Jack Frost Company, and August 3 developed bacillary dysentery and was brought to the Floating Hospital.

J. W., 4 years of age, lived in another part of the city in a sanitary home and under intelligent care, and there were no cases of bacillary dysentery in the neighborhood. The child ate a Jack Frost icecream cone July 22. Symptoms developed July 24, and he was taken to the Children's Hospital, where he died. Dysentery bacilli were isolated from the stools of both children and were of the same type.

August 3, a sample of icecream was obtained from the Jack Frost Icecream Company. There were seven million bacteria per cubic centimenter, with colon bacilli in 1/1,000 of a cubic centimeter. Dysentery bacilli of the Flexner type were actually isolated from the sample of icecream. This is the only instance in which we were able to isolate dysentery bacilli from icecream cones, though total bacterial counts and colon bacilli counts always showed very undesirable conditions.

Water.—The one outbreak that could probably be attributed to water was a short but severe one.

W. M., 3 years old, lived in a large suburban home in a newly constructed portion of the city, with ideal conditions for outdoor exercise. The child had not been away from home, and had played with no children except his older sisters. The building of new streets had opened up a spring which filled a pool in the roadside in front of the house, and from this the workmen used to drink, and sometimes also washed their hands in it. One day the child followed their example. There had been clogging of the nearby house sewers eight to ten days before, and the sewage had been pumped from the cellar into the street about 100 feet above the spring. Aug. 4, four days after the child drank from the spring, symptoms of dystentery developed, and he died

in three days. The child was nursed by his father and mother, and the older children frequently came to his bedroom. August 7 the mother and a 6-year-old sister developed dysentery, and the father became ill August 8. All were severely infected, but eventually recovered. The blood from both father and mother developed agglutinins for the Hiss Y-type of dysentery bacillus in dilutions of 1 to 320. This same type was isolated from the father's stool. A careful study was made of the food eaten by the family, and all other possible sources of infection, and the conclusions reached were that the three secondary cases were probably contacts from the baby, and that the baby was infected from drinking the water in the spring. This water was analyzed bacteriologically, August 24. Total bacterial count, 2,700 per c.c. Coli in $\frac{1}{100}$ of a cubic centimeter. Careful search was made for dysentery bacilli, but none were found.

The Shiga Epidemic.—There was one epidemic of dysentery due to the Shiga bacillus which threaded a devious and devastating path through several communities and gave us the best single example of the various modes of transmission of bacillary dysentery.

Baby H. P., 2 years of age, was taken to Lawrence, Mass., July 14, where he was given some icecream. The child developed acute enteritis, July 16, was taken to the Gale Hospital July 19, and died. The father developed diarrhea July 19, the mother July 20, and another child July 22. All were moderately ill, and the father continued to work throughout his illness. Mr. H. P., Sr., was a milker in the R. dairy, which sent almost its entire milk supply to a Fresh Air Home for children in Haverhill. There were about seventy-five children in this summer camp, from 7 to 14 years of age, most of them coming from Boston and vicinity. July 24 the first case of bacillary dysentery developed in the home, and within four days there were twenty more cases, all quite ill. The superintendent at once closed the Fresh Air Home and sent all the children to their homes.

One of the children, L. R., 9 years of age, was sent to her home in Pine Heights, an unsanitary Boston suburb. She was very ill and remained at home only three days, after which she was taken to the Children's Hospital. She remained at home long enough, however, to infect her two sisters, aged 5 and 7 years, and her brother, aged 11 years, who developed symptoms August 3, August 5 and August 6. August 8 all of them were taken to hospitals, the two younger being quite ill. A neighbor had helped in the care of these children, then returned to her home and prepared her husband's supper. August 9 he developed a moderately severe dysentery.

The dejecta from the C. children was thrown down the pit of an open privy without disinfection. August 12, a neighbor's child, L. E., 2 years old, living directly across the street from the C.'s, developed bloody dysentery and died in three days. This family had not come in contact with the C. family, but since flies were so prevalent, both in the E. kitchen and in the C. privy, I believe the infection was carried across the street by flies.

August 12 and 13 three adult neighbors in one family all developed severe diarrhea, which persisted for a few days only. These cases had not been in contact with the C. family and are possible fly infections.

August 20 the baby brother of L. E. developed a moderate diarrhea, but dysentery bacilli were never recovered from his stools. August 21 R. G., a 2-year-old child living next door to L. E.'s, developed bacillary dysentery. He had been playing with L. E. the week before and probably was a contact case. This child was brought to the Floating Hospital, August 25, and died that night. Shiga dysentery bacilli were isolated from his intestinal wall, and from this case our epidemiologic investigation of the Shiga epidemic began, gradually developing the various details that have been described (Charts 4 and 5).

CONCLUSIONS

1. Bacillary dysentery is a readily communicable disease which may be spread in a community by means of contact with an acute case or a carrier, by means of food, as milk, condensed milk and icecream, by water, and by flies.

2. The sporadic summer bacillary dysentery of infants may be transmitted to older children or to adults. Though the disease is severe in the infant, it is usually mild in older children or adults. As a general rule, the older the child, the milder the disease.

3. The dysentery bacilli from the stool of an adult with a mild case of dysentery may produce a rapidly fatal dysentery in infants. Thus the menace of the mild adult case to the community is considerable.

4. Bacillary dysentery is rarely found in a nursing baby.

5. Hospital contact cases are not uncommon. The disease is very readily transmissible by direct contact, and no hospital has a right to admit patients with dysentery unless it can make provision for their isolation.

HYPERTENSION IN NEPHRITIS IN CHILDHOOD, WITH A STUDY OF NINETY-THREE CASES *

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A recent and unusual case of high blood pressure in nephritis in a boy of 10 stimulated a review of the literature to ascertain the frequency with which, and to what degree, hypertension occurred in nephritis in children. Considering the attention blood pressure has received in the nephritis of adults, we were immediately struck by the scarcity of literature relating to blood pressure in nephritis occurring in the early years of life.

Shaw[1] reports three cases of acute nephritis in children with blood pressure readings, and concludes that "hypertension in acute nephritis, so constant in adults, is not so marked in children." Gordon[2] reports the blood pressure in nine cases, seven of which were acute nephritis and two chronic cases with acute symptoms superimposed. He found that the blood pressure in acute nephritis is elevated, and that the increase may be very great, one of his cases having a pressure of 180 mm. Hg. He also pointed out that the cases with the highest pressure show very little edema, but have large amounts of blood in the urine. The large amount of blood, he believes, is due to a rupture of renal capillaries by increased pressure. Barber[3] reports three cases of chronic interstitial nephritis in children. The blood pressure was below 100 mm. Hg on several occasions in the one case that he tested. Wessler[4] found a latent hypertrophy of the heart occurring in nephritis in children which he believes is secondary to arterial hypertension. Bugge[5] asserts that the blood pressure in both orthostatic and nephritic albuminuria is usually normal. Bass and Wessler,[6] after analyzing twenty-six cases of orthostatic albuminuria, conclude that the blood pressure differs but little from normal. Thus, while increased tension is expected, according to most authors, the evidence is not conclusive, and no figures have been reported giving the constancy or extreme limits of the increase.

In the records of the Massachusetts General Hospital and the medical service of the Children's Hospital, ninety-three cases of nephritis

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* From the Children's Medical Department, Massachusetts General Hospital, and the Medical Service of the Children's Hospital, Boston.

1. Shaw, H. L. K.: Albany Med. Ann., 1900, **21,** 88.
2. Gordon, Lennox: Arch. Pediat., 1911, **28,** 343.
3. Barber, Hugh: Brit. Med. Jour., Nov. 8, 1913, p. 1204.
4. Wessler, H.: Arch. Int. Med., 1914, **14,** 517.
5. Bugge, J.: Norsk Mag. f. Laegevidensk., 1913, **74,** 1601.
6. Bass and Wessler: Arch. Int. Med., 1914, **13,** 39.

in children between the ages of 2 and 12 years were found in which blood pressures had been recorded. Sixty-five of these cases were diagnosed as acute nephritis and twenty-eight as some form of chronic nephritis. No attempt has been made to subdivide the cases of chronic nephritis into the different pathologic classes. These cases have been taken as the basis of this report. They cover a period of several years and represent the observations of numerous men. Deductions from these records are open to criticism on several points. In no case is the size of the cuff used mentioned, the importance of which has been pointed out by Judson and Nicholson[7] and P. Wolfensohn-Kriss.[8] The personal factor in blood pressure observations has been pointed out by Kilgore[9] and by Kilgore, Berkley, Rowe and Stabler.[10] The importance of the phase taken for the reading has been pointed out by numerous observers. We feel, however, that some value may be attached to these findings, and it is hoped that this report may lead to further investigation along the same line in which all of these factors have been properly controlled.

The blood pressure of normal children has been studied by several observers from different points of view. As early as 1900 Shaw[1] reported 400 observations on forty-five children, using Gartner's tonometer. P. Wolfensohn-Kriss[8] and M. Michael[11] report the relation of the blood pressure to the body weight and the height in normal children. Other investigators who should be mentioned are Cook,[12] Stowell and Gordon,[13] Gordon,[2] Nirrnheim,[14] Oppenheim and Bauchwitz,[15] Kaupe,[16] Mello Leitao,[17] Katsenberger[18] and Rolleston.[19] The most recent and most exhaustive work is that of Judson and Nicholson.[7] These authors give a complete summary of the work up to date and should be consulted by those interested in the subject. They also report a series of 2,300 observations of their own which they have tabulated, the pressures being those of normal children between the ages of 3 and 15 years. Their results are taken as a standard for comparison in this paper, though as stated above, we do not claim such accuracy as theirs.

7. Judson, C. F., and Nicholson, P.: Blood Pressure in Normal Children, Am. Jour. Dis. Child., 1914, **8,** 257.
8. Wolfensohn-Kriss, P.: Arch. f. Kinderh., 1910, **53,** 332.
9. Kilgore, E. S.: Arch. Int. Med., 1915, **16,** 934.
10. Kilgore, Berkley, Rowe and Stabler: Arch. Int. Med., 1915, **16,** 927.
11. Michael, M.: A Study of Blood in Normal Children, Am. Jour. Dis. Child., 1911, **1,** 272.
12. Cook, H. W.: Am. Jour. Med. Sc., 1903, **125,** 433.
13. Stowell: Albany Med. Jour., 1900.
14. Nirrnheim, E.: Kinderheilsanst; Dresden Dissertation, Kiel, 1913. Also Monatschr. f. Kinderh., 1914, **12,** 20.
15. Oppenheimer and Bauchwitz: Arch. f. Kinderh., 1905, **42,** 415.
16. Kaupe, W.: Monatschr. f. Kinderh., 1910-1911, **9,** 257.
17. Leitao, Mello: Arch. de med. d. enfants, February, 1913.
18. Katsenberger, A.: Ztschr. f. Kinderh., 1913, **9,** 167.
19. Rolleston, J. D.: Brit. Jour. Dis. Child., 1911, **8,** 433.

For the purpose of comparative study the cases here reported have been grouped as follows:

1. Nephritis in general (including all cases regardless of type).
2. Acute nephritis, sixty-six cases.
3. Chronic nephritis, twenty-seven cases.

Table 1 shows the distribution of these cases as to age, type of nephritis and the number of systolic and diastolic observations for each age.

Clinical notes in all cases but one have purposely been omitted. The following case, however, is given in detail because of certain unusual features.

TABLE 1.—AUTHOR'S CASES SHOWING TYPE OF NEPHRITIS AND NUMBER OF BLOOD PRESSURE OBSERVATIONS

Age	Total Number Cases	Number of Acute Cases	Number of Chronic Cases	Number of Systolic Observations	Number of Diastolic Observations	Total Observations
2	3	2	1	3	3	6
3	4	3	1	6	5	11
4	11	10	1	24	15	39
5	9	9	0	16	16	32
6	9	7	2	13	11	24
7	11	7	4	17	8	25
8	10	6	4	34	16	50
9	14	12	2	32	12	44
10	8	1	7	20	6	26
11	10	7	3	25	20	45
12	4	2	2	26	1	27
	93	66	27	216	113	329

REPORT OF CASE

History.—M. F., boy, aged 10 years, entered the Massachusetts General Hospital for diagnosis. The family history was negative, and there was no evidence of specific disease.

Past History.—Full term, normal delivery, normal at birth, and weighed 8 pounds. No coma or convulsions. Breast fed for three weeks and then discontinued because the child had three convulsions (general rigidity with clonic contractions). He was subsequently fed on modified cow's milk and did poorly. He had measles at 6 years, whooping cough at 6½ years, mumps when 7 and chickenpox when 7½ years of age. He had not had scarlet fever, diphtheria, rheumatism, chorea or tonsillitis.

Present Illness.—Complaint, headache and failing vision. The patient was apparently perfectly well up to two months before entry to the hospital, when his mother noticed that he held papers close to his eyes when reading. Six weeks previous to admission to the hospital his teacher reported that his vision

was imperfect, but he continued in school three weeks after this and then had glasses fitted by an optician, with no improvement. An oculist consulted shortly after this offered no satisfactory explanation. Since onset of present illness he had had occasional attacks of headache and vomiting. The headaches were always frontal, sometimes radiating to the occiput. They came at no definite time, being present at times when he awoke in the morning and sometimes coming on during the day. Occasionally he had headache after reading. During the week previous to entering the hospital the headaches were unusually severe and were accompanied by vomiting. For two days he had had no pain. The vomiting bore no relation to meals and was definitely propulsive. There was no marked change in disposition, though the mother thought the boy had been more "cranky" recently. He had no staggering, twitchings, convulsions, diplopia, blurring of vision, dyspnea, cyanosis or edema. No nocturia, frequency, bloody or smoky urine had been noted. The mother believed his eyes had been puffy at times, but was not sure.

Physical Examination.—A fairly well developed, thin, sallow, white boy of about 10 years. Pupils equal, regular; react to light and distance. There was a lateral nystagmus and a marked albuminuric retinitis. Tonsils moderately enlarged. Multiple shotty glands palpable in cervical, axillary and inguinal region; epitrochlears palpable. Left border cardiac dulness 9 cm. to left of midsternal line; right border 3.5 cm. to right of midsternal line. Apex impulse diffuse and forcible. Sounds regular, slow and of good quality; no murmurs. Aortic second sound was greater than pulmonic second sound, and loudly accentuated. At aortic area there was a gallop rhythm. Palpable and visible impulse in second interspace, 3.5 cm. to right of midsternal line. Palpable pulsation in suprasternal notch. Pulses equal, synchronous and of high tension. Arterial wall distinctly palpable after pulse had been shut off by compression. Lungs normal. Abdomen normal, liver and spleen not palpable. Extremities normal, no edema. Knee jerks equal and exaggerated. Achilles reflexes active, with suggestion of clonus on the right. Physical examination otherwise normal. The blood pressures in this case on entry were, systolic 250 mm. Hg, and diastolic 210 mm. Subsequent readings were

Systolic	250	218	210	210
Diastolic	190	190	180	180

Clinical Notes.—On a dry diet (360 c.c. fluid intake) 1,560 c.c. of urine were excreted with a specific gravity of 1.005, which indicated an inability of the kidneys to excrete salts in a concentrated form.

The carbon dioxid tension of the alveolar air was 42.8. The urine became neutral in reaction after the administration of 1 gm. of sodium bicarbonate by mouth. Both of these tests showed the absence of acidosis.

After the administration of 10 gm. of urea by mouth the urine for the following twenty-four hours contained but 5.3 gm. (urease method), indicating a marked decrease in the ability of the kidneys to excrete nitrogen.

Nonprotein blood nitrogen, 40 mg. per 100 c.c. of blood.

Urine: Sp. Gr. 1.005; albumin, heavy trace; sugar, 0; acetone, 0; sediment showed many hyaline and granular casts; no blood cells.

M. F. was discharged unrelieved with a diagnosis of chronic nephritis and an unfavorable prognosis given to the parents. Death occurred at home three weeks after leaving the Massachusetts General Hospital. Unfortunately no postmortem examination was made.

This case shows that the blood pressure in nephritis in childhood may be tremendously increased, even reaching a point usually seen only in well marked adult cases. Hypertension of this degree is unusual in children, and in our series only seven cases show a pressure of 150 mm.

Hg or above, four of these being acute and three chronic nephritis. Only five additional cases had pressures as high as 140 mm. Hg, three acute and two chronic cases.

Headache, so prominent a feature in this case, is an uncommon symptom. It is mentioned in but one other case in the entire series, a child, aged 10 years, with chronic nephritis, uremia, temporary blindness, and having a blood pressure of 170 mm. Hg.

Changes in the fundus secondary to nephritis apparently are very uncommon in childhood. We have found no mention of such changes in the literature, and such changes were found in but one other case in the series, a boy, aged 10 years, with a systolic pressure of 210 mm. Hg, who died two weeks after leaving the hospital. These two cases are the only ones in the entire series of ninety-three cases having systolic pressures of over 200 mm. Hg. In the case recorded there was a well marked albuminuric retinitis, with large patches of exudate and numerous small hemorrhages in each eye. Whether these changes are frequently present and are not looked for, or are extremely rare, it is of course impossible to say. It seems probable, however, that the condition but rarely occurs. This condition in adults is generally considered a prognostic sign of some importance, and the rapid, fatal outcome in both of these cases suggests that it may carry with it a similar prognosis in children.

It is of interest to note that in this case, with a tremendously increased blood pressure, there were no blood elements found in the urine.

As is not infrequently the case in nephritis in children, no etiology for the nephritis could be found in this case.

COMPARISON OF THE BLOOD PRESSURES OF NEPHRITIC AND NORMAL CHILDREN

Believing that the blood pressure is raised in the nephritis of children, it becomes of interest to know the constancy and extent of this rise. In Figure 1 we have shown the averages of all the blood pressures in the ninety-three cases of nephritis compared graphically with the normal figures of Judson and Nicholson. This figure shows that although there are slight variations, there is a definite increase in both systolic and diastolic blood pressures in nephritis when compared with the normal blood pressure for the corresponding age. In our series this increase averages about 20 mm. Hg for systolic and about 10 mm. for diastolic readings.

The diastolic pressures showing a less marked increase over the normal, indicate that in nephritis in childhood there is an increase in the pulse pressure. The extent of this increase is shown in Table 2, the normal figures being those of Judson and Nicholson. It is readily

seen that this increase is not a constant factor and varies between the wide limits of 0.1 and 21. The normal pulse pressure as given by other observers also show wide variations from those given by Judson and Nicholson, and for this reason we feel that further studies are necessary definitely to decide the effects concerning the pulse pressure in nephritis in childhood.

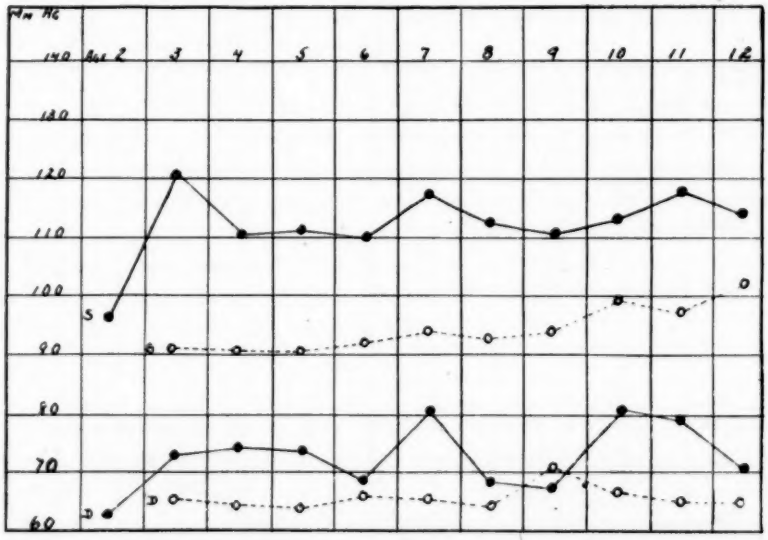

Fig. 1.—Curves showing averages of the blood pressures in ninety-three cases of nephritis compared with the normal figures of Judson and Nicholson. S = systolic; D = diastolic; O—O = normal; ●—● = nephritis.

TABLE 2.—Normal Pulse Pressures Compared to Those of Nephritis

Observers	Age, Years										
	2	3	4	5	6	7	8	9	10	11	12
Normal pulse pressure, Judson and Nicholson...	—	26.2	26.7	26.9	25.3	26.9	28.9	23.3	32.1	31.5	37.1
Nephritic pulse pressure, Berkley and Lee.....	34	47.2	35.1	37 0	30.5	36.5	44.0	44.3	32.2	38.4	42.6
Increase over normal.....	—	21.0	8.4	10.1	5.2	9.6	15.1	21.0	0.1	6.9	5.5

COMPARISON OF THE BLOOD PRESSURES OF CHRONIC AND ACUTE NEPHRITIS

In order to ascertain whether in children chronic nephritis showed higher blood pressures than acute nephritis, we have in Figure 2 compared the average blood pressures of our patients in these two groups. The differences are not sufficient and are too irregular to warrant

drawing definite conclusions. It would seem that there is no increase in the blood pressure of chronic nephritis over that of acute nephritis in childhood. It is possible, however, that in a larger series some difference might be shown. It was found impossible to study the effect of such factors as severity, type of involvement, or duration of the disease in our cases. The highest systolic pressure among our acute cases was 190 mm. Hg (in a child of 4) and among the chronic cases, 250 mm., the case above reported.

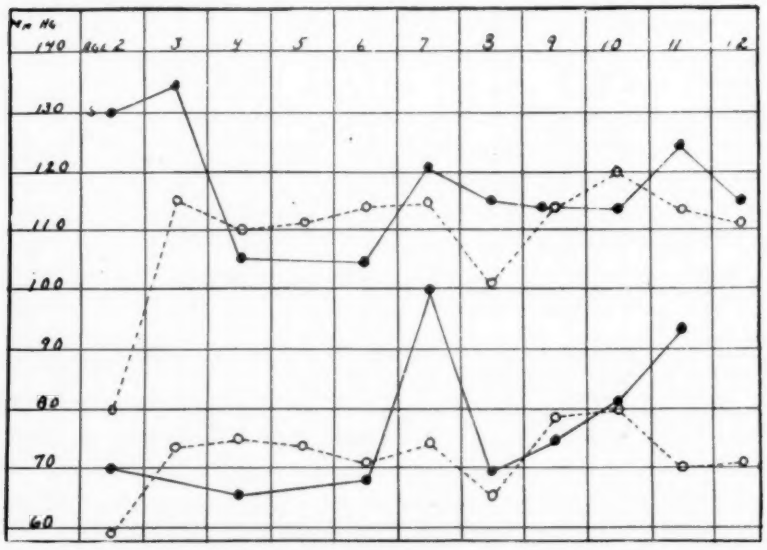

Fig. 2.—Curves comparing the blood pressures of acute nephritis with those of chronic nephritis. S = systolic; D = diastolic; o—o = acute nephritis; ●—● = chronic nephritis.

EDEMA AND BLOOD IN THE URINE WITH RESPECT TO BLOOD PRESSURE

Since Gordon has stated that patients showing the highest blood pressures had comparatively little edema and a large amount of blood in the urine, we reviewed the forty-one cases from records of the Massachusetts General Hospital with these points in view. Thirty-three patients showed a more or less marked edema, while eight showed very little or none. The average blood pressure in those patients having edema was 123.8 mm. Hg. The average systolic blood pressure of those with little or no edema was 112 mm. Hg. Twenty patients with large amounts of blood in the urine had an average systolic blood pressure of 112 mm. Hg, while twenty-one having little or no blood had an average of 126 mm. Hg. In each instance in which the systolic blood pressure has averaged above 150 mm. Hg the urine has been

found to show but little blood. The degree of edema in our patients having a systolic pressure of 150 mm. or over has been found to vary from "very slight" to "well marked." These results show that there is probably no definite relation between the increase in the blood pressure and the amount of edema present or the amount of blood in the urine, as suggested by Gordon. The amount of blood we believe is relative to the severity of the pathologic process present rather than to an increase in blood pressure. The amount of edema probably varies with the ability of the kidneys to excrete salts.

URINARY FINDINGS COMPARED WITH BLOOD PRESSURE

We have reviewed the urine charts in these same cases to find, if possible, any relation between the increase in blood pressure and the amount of albumin or number of casts in the urine. Blood pressures were also compared with the specific gravity of the urine. So far as we were able to determine, no relation exists between the blood pressure and any of these factors. That the urinary findings bear no relation to the pathology of kidney lesions has been shown by Stark.[20]

SUMMARY

From a study of blood pressure observations in ninety-three cases of nephritis in children between the ages of 2 and 12 years, we may say that

1. The blood pressure is elevated in the nephritis of childhood, and occasionally to a marked degree. This applies to both acute nephritis and chronic nephritis.

2. Systolic and diastolic pressures are not increased to the same degree, the former averaging about 20 mm. Hg, and the latter about 10 mm. above normal.

3. The pulse pressure is increased, but the factor is not constant.

4. The blood pressure in chronic nephritis shows no constant elevation above that of acute nephritis.

5. The blood pressure may, in rare instances, be of prognostic value.

6. No relation has been found to exist between the blood pressure and the urinary findings.

7. Patients having marked edema showed a slightly higher average blood pressure than those with little or none. This difference is not great enough to warrant definite conclusions.

8. Albuminuric retinitis is probably not common even in cases showing a marked increase in blood pressure.

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20. Stark, J. R.: Jour. Lab. and Clin. Med., November, 1916, p. 134.

PROGRESS IN PEDIATRICS

REVIEW OF RECENT LITERATURE ON CONDITIONS OF ABNORMAL METABOLISM IN INFANTS *

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ACUTE DISTURBANCES OF NUTRITION

Metabolism Studies in "Dyspepsie" and "Intoxikation."—Jundell[1] has studied the fat, nitrogen and mineral metabolism in two cases of "Dyspepsie" and in two cases of "Alimentären Intoxikation." The four infants were quite young, their ages ranging from 4 to 8 weeks, and all of them developed the conditions investigated while taking buttermilk to which was added a large amount of sugar. The sugar content of the milk was 8 per cent., and in one instance, 10 per cent. The food was continued through the periods during which the metabolism was studied. The symptoms of the condition designated "Dyspepsie" were severe diarrhea, five to ten thin, slimy or watery stools daily, occasional vomiting and stationary or declining weight. The onset of the symptoms was fairly abrupt. Two experimental periods of several days' duration were obtained from each infant. In the case of the infants developing "Intoxikation" there was, with the diarrhea, an abrupt and rapid loss of weight, an initial rise of temperature, and then a deepening of respiration, stupor and the appearance of sugar in the urine. A single twenty-four hour period was obtained from each of the infants, after which they were given water and then protein milk, and in both instances gradually recovered. Although so short a metabolism period is not entirely satisfactory, the author maintains that the disturbances of metabolism in "Intoxikation" progress so rapidly that the figures obtained are acceptable. In reviewing the author's results, normal figures given for comparison are indicated by enclosing them in parentheses. These normal figures are those provided by the author or else they were obtained from Tobler and Bessau.[2] Since so many factors in normal metabolism are variable, such figures possess only an approximately "normal" value. All of the absolute figures given are for per diem quantities.

1. Jundell: Ztschr. f. Kinderh., 1913, **8**, 235.
2. Tobler and Bessau: Allgemeine Pathologische Physiologie der Ernährung und des Stoffwechsels im Kindesalter, Weisbaden, 1914.

The author's results show strikingly the effect of diarrhea in decreasing the volume of urine excreted. In "Dyspepsie" the average urine volume was 117 c.c. and in "Intoxikation" it was 40 c.c. (normal 500 to 600 c.c.). The amount of stool in "Dyspepsie" was 250 gm., in "Intoxikation" it was 312 gm. (normal 20 to 50 gm.). Urine and stools together amounted in "Dyspepsie" to 370 gm. and in "Intoxikation" to 350 gm. (normal 500 to 700 gm.), showing that in diarrhea less water is carried from the body in the stools and urine together than normally. That this is not due to a lack of water intake is shown by figures for urine and stool excretion per 100 c.c. of food. They were, for "Dyspepsie," 54 gm., for "Intoxikation" 60 gm. (normal 64 gm.). If diarrhea is accompanied by a desiccation of the tissues, as is often inferred, this cannot be due to the watery stools per se, and can only be explained by assuming a greater than usual water loss through the skin and lungs. The absorption of nitrogen from the intestine in percentage of nitrogen in the food was, in "Dyspepsie," 78 per cent., as compared with 90 per cent. absorbed by normal infants. The nitrogen retained in percentage of intake was in one instance 28 per cent., in the other 49 per cent. (normal 33 per cent.). The absolute retention was 0.68 gm. and 1.22 gm. (normal 0.8 gm.). By an increased retention the body therefore managed to obtain its nitrogen need in spite of the diarrhea. In the "Intoxikation" cases the absorption of nitrogen was much lower than normal — 58 per cent and 34 per cent. of the intake. In the first instance there was an absolute retention of 0.63 gm., or 32 per cent., of the intake; in the second, the nitrogen balance was negative, showing a loss of 0.34 gm. The absorption of fat was in "Dyspepsie," 57 per cent. of the intake (normal 90 to 98 per cent.). In "Intoxikation" the absorption was 46 per cent. and — in the more severe case — only 12 per cent. The utilization of fat is therefore lower than normal in "Dyspepsie" and very low in severe "Intoxikation." Analysis of the stool fat showed in both "Dyspepsie" and "Intoxikation" about the same partition into neutral fat, fatty acids, and soaps. In average there was found 20 per cent. of the total fat, as neutral fat, 63 per cent. as fatty acids and 17 per cent. as soaps. Reliable normal figures, especially for the fatty acid and soap ratio, have not been established. Nieman found in a normal 3½ months infant practically no neutral fat in the stool, 97 per cent. of the total fat as fatty acids and only 3 per cent. as soaps. The retention of total ash was in average in one case of "Dyspepsie" 20 per cent. of the ash in the food, and in the other 9 per cent. (normal 11 to 23 per cent.). The total mineral balance was negative in both cases of "Intoxikation." As regards the constituents of the ash, the retention of calcium and phosphorus was least affected by the diarrhea, whereas there was marked loss of the alkaline metals, sodium and potassium. Mag-

nesium was not determined. In "Dyspepsie" the retention of CaO was 0.27 gm. and 0.248 gm. (normal 0.13 gm. to 0.23 gm.). In "Intoxikation" it was 0.202 gm. and 0.026 gm. There was thus in spite of the diarrhea a normal CaO retention except in the more severe of the 'Intoxikation" cases. A positive balance for P_2O_5 obtained both in "Dyspepsie" and "Intoxikation," although the amounts retained were possibly somewhat less than normal. The balance for K_2O was positive in both cases of "Dyspepsie," 0.18 gm. and 0.13 gm. being retained (normal 0.18 gm. to 0.32 gm.). In "Intoxikation" there was a negative balance with a loss of 0.15 gm. and 0.35 gm. In one case of "Dyspepsie" the Na_2O balance was positive, 0.051 gm. (normal 0.08 gm.?), in the other it was just negative, — 0.005 gm. It was markedly negative in both cases of "Intoxikation," — 0.27 and — 0.31. The chlorin balance was positive in one case of "Dyspepsie," the amount retained being 0.046. In the other case there was a loss of 0.064 gm. In both cases of "Intoxikation" the balance was negative, — 0.112 and — 0.250. These results are in accord with the finding by Holt, Courtney and Fales[3] that there is in diarrhea a relatively much greater loss in the stool of chlorin and of the alkalies than of calcium and magnesium.

The author regards his results as confirming Finkelstein's definition of "Dyspepsie" as a disturbance entirely local in character, limited sharply to the gastro-intestinal canal and not directly interfering with nutritional processes going on within the body. In contrast there is in "Intoxikation" a general upset of metabolism, with destruction of body tissue, as indicated by a negative nitrogen and mineral balance. He explains the positive nitrogen balance in one of the "Intoxikation" cases as most probably due to an inability of the organism to excrete effete nitrogen. He believes that he has established Finkelstein's view that "Dyspepsie" and "Intoxikation" are unrelated entities by showing that the disturbances in metabolism are in the two conditions distinctly different. It is much easier, however, unless one desires to support Finklestein's preconception, to make just the opposite inference from the author's results, namely, that the disturbances detected in "Dyspepsie" could by progressing simply in degree become those obtaining in the condition designated "Intoxikation."

Relation of Volatile Fatty Acids in the Intestine to Diarrhea.— Bahrt and co-workers have investigated the possibility of a causative relation of the volatile fatty acids in the intestine to diarrhea. Their evidence in this direction is much more nearly quantitative than that which has been presented by other workers. Bahrt and Bamberg[4] by experiments with dogs demonstrated that the lower or volatile members

3. Holt, Courtney and Fales: Am. Jour. Dis. Child., 1915, **9**, 213.
4. Bahrt and Bamberg: Ztschr. f. Kinderh., 1912, **3**, 322.

of the fatty acid series are capable of increasing peristalsis when administered in relatively small amounts. The degree of effect produced by the same sized dose of the various volatile fatty acids they found to be roughly inversely proportional to their molecular size. Considerably more butyric or caproic acid had to be given to obtain an increase in peristalsis than of acetic acid, the lowest member of the series present in the intestine. Using the bismuth and Roentgen-ray method of Cannon, they studied the effect on stomach and intestinal peristalsis of the administration of volatile acids in the food. They found that 0.2 to 0.5 gm. per kilo of acetic acid caused an increase of peristalsis usually with diarrhea and occasionally with vomiting. When less than the effective dose was given they noted a well-marked defensive effort on the part of the pylorus, the orifice opening much less frequently than normal and thus providing more time for the secretion of digestive juices to the extent necessary for neutralization of the acid entering the duodenum. In another series of experiments they administered the acids below the pylorus by injecting them through a duodenal fistula. Small amounts were injected at short intervals, mixed with chyme. The amounts of acetic acid needed to produce diarrhea by this method of experimenting was found to be 0.04 to 0.16 gm. per kilo, very much less than when the acid was given by mouth.

The concentration of free volatile fatty acid in sour milk and developing in the infant's stomach during digestion was then studied.[5] In sour milk the concentration of lower fatty acids (chiefly acetic) measured with tenth-normal NaOH was found to be 8 to 10 c.c. per 100 c.c., and in stomach contents (mostly butyric acid) 10 to 22 c.c. The fatty acids in the stomach were not found to be increased in dyspepsia with diarrhea. The concentration in sour milk was one-tenth and in the stomach contents one-fifth that needed to cause an increase in peristalsis in dogs when given by mouth. The authors conclude that if diarrhea is to be related to free volatile fatty acids it must be assumed that they are produced for the most part in the intestine itself; and here, as they have shown, a much lower concentration than in the food is effective because of the defense of duodenal alkalinity afforded in the latter case by the pyloric reflex. That there is a production of volatile acids in the intestine has been shown by stool analysis. Edelstein and Csonka[6] found, for instance, 0.7 gm. acetic acid and 0.125 gm. butyric acid in 100 gm. stool from a normal breast fed infant. That the volatile acids are produced chiefly through the agency of intestinal bacteria is shown by the relatively much larger

5. Huldschinsky: Ztschr. f. Kinderh., 1912, **3**, 366.
6. Edelstein and Csonka: Biochem. Ztschr., 1912, **42**, 372.

amount of acetic than of butyric acid. The volatile acids cannot, of course, exert an effect on peristalsis unless they are free. Bahrt and McLean[7] have made an extensive study of the amounts of free and combined volatile fatty acids found in the stools of normal infants and of infants with diarrhea. They distilled altogether some 140 stools by the Edelstein-Weldeschen method.[6] Expressed as cubic centimeters of tenth-normal NaOH per 100 gm. stool, they found, in average, from stools of normal breast fed infants 22 c.c. free and 111 c.c. combined volatile acid. With various modifications of cow's milk there was found in stools from normal infants no free volatile acids (except with Friedenthal's milk, and in one of five instances with buttermilk). The amount of combined volatile acid was in average 90 c.c. The addition of sugar to breast milk doubled the amount of free volatile acid in the stools, but an increase in the sugar in the cow's milk modifications did not cause the appearance of free volatile acids in the stools. In a series of infants with "Dyspepsie," 21 per cent. of the volatile fatty acids were free when the food was breast milk, and 10 per cent. free when the infants received cow's milk. In examination of another series of stools from infants with severe "enterocatarrh," and in many instances presenting symptoms of "Intoxikation," there was found on breast milk 30 per cent. of the volatile fatty acids free, and on cow's milk, 38 per cent. free. The diarrheal stools from both "Dyspepsie" and "enterocatarrh" contained about the same total amount of volatile acids per 100 gm. fresh stool as was found in stools from normal infants. The absolute amount of volatile acids excreted must, however, have been much greater than normal, since in diarrhea the volume of the stool is two to six times normal. The authors believe that this large production of volatile acids may well tend to exceed the supply of base in the food and intestinal secretions. From their duodenal fistula experiments with dogs the authors are convinced that the 30 to 50 c.c. (tenth-normal NaOH) free volatile acids per 100 gm. stool found in "Dyspepsie" and "enterocatarrh" represents a concentration which if present in the small intestine of an infant would be much more than sufficient to cause an active increase in peristalsis, and they infer that the presence in the stools of such an amount of free volatile acids indicates that they exist in the small intestine in sufficient concentration to provide the immediate cause of diarrhea. They are, of course, unable to supply direct proof of their theory, and its correctness must be regarded as problematical. It is conceivable that in diarrhea a large part of the volatile acids could be produced in the large intestine and their presence in the stools represents a result rather than a cause of the condition. As regards the cause in the first instance of the "souring

7. Bahrt and McLean: Ztschr. f. Kinderh., 1914, **11,** 143.

of the chyme," their evidence is against assuming an ingestion of free volatile acids or their production in the stomach in sufficient amount. They are inclined to regard a disturbance of the pyloric reflex as the initial cause of diarrhea. They suggest, for instance, that overfeeding might lead to an abnormally rapid passage of food into the small intestine and thereby supply the intestinal bacteria with an unusual amount of material from which it would be possible for them to produce acid to an extent in excess of available base.

The authors wish also to relate chronic nutritional disturbances of the type of Czerny's "Milchnärschaden" to the presence in the intestine of the volatile acids. In this condition their concentration is not regarded as being so high as in "Dyspepsie," but is sufficient to cause an increase in peristalsis in the small intestine, which is indicated by a decreased fat absorption and an increased nitrogen excretion. The stimulus to peristalsis is, however, not strong enough to involve the large intestine, and the stool mass remains there long enough to permit the absorption of water, of the alkali salts, and the alkali present in combination with the higher fatty acids, which is replaced by calcium and magnesium supposed to be excreted into the intestine at this point. The stools resulting are typical, more or less dry "soap stools" containing more calcium and magnesium and very much less sodium and potassium than diarrheal stools. In diarrhea the stimulus to peristalsis is of such degree that the large intestine is also involved so that the stool mass does not remain there long enough to permit of salvage of the alkalies. The authors insist that the building of insoluble soaps which takes place in the large intestine in "Milchnärschaden" is only an incidental result of the condition. They and other workers have shown that the amount of higher fatty acids in soap stools is quite insufficient to bind all of the calcium and magnesium present and should not therefore be regarded as bearing a causative relation to the loss of these metals. They refer the loss of the earth alkalies to the increase in intestinal secretion and of persistalsis due to the presence of free volatile acids, resulting in the carrying into the large intestine of large amounts of sodium and potassium which are there saved at the expense of calcium and magnesium. The authors discuss the quantitative relation of the lower fatty acids to the base loss obtaining in diarrhea. From the values for volatile fatty acids obtained in their investigation of diarrheal stools they have calculated, using a one-half maximal figure, that the stool from one of the infants with severe "enterocatarrh" studied by Jundell[1] may have contained enough volatile acid to combine with 3 gm. of base (reckoned as K_2O). In this case of Jundell's $CaO + K_2O$ and Na_2O amounted to 1.2 gm. They conclude that there is probably a sufficient amount of volatile fatty acids present

in diarrheal stools to bind all the base present. They maintain, however, that the cause of the base loss is not related to the base-claiming value of the volatile fatty acids, but to their effect in stimulating the secretion of alkali and preventing its absorption by increasing peristalsis.

A Specific Toxic Substance a Cause of Diarrhea?—The most recent effort to relate diarrhea to the presence in the intestinal canal of a particular toxic substance has been made by Mellanby.[8] He believes that a substance known as βimidozolyethelamine, and for which he suggests the abbreviation βi, may, with great probability, be held accountable for the more acute and severe types of diarrhea and vomiting in infants and children. This substance can be derived from the amino-acid histidin simply by the removal of CO_2, and is related to products of intestinal putrefaction such as cadaverin and putrescin, which are known as ptomains and are supposed to be capable of producing symptoms of food poisoning. βi was first isolated from ergot by Barger and Dale,[9] and they later demonstrated its presence in the alimentary canal of normal animals. The author is able to obtain βi from histidin by the action of a certain bacillus which can be isolated from the feces of human beings.[10] Experiments with animals have shown it to be capable of producing diarrhea and vomiting, fall of systemic blood pressure, depression of the respiratory center, coma and death. Mellanby has studied in cats the conditions which favor the absorption of βi from the intestinal canal. He found that the presence of food (milk or meat) or of water in the intestine greatly decreased the rate of absorption of the substance. Injection of large amounts of Ringer's solution into the circulation had the same effect. Absorption was most rapid from the empty intestine and was further increased when the water content of the body was reduced by bleeding. He found absorption of βi most rapid in the region of the cecum, and that apparently it was not taken up at all from the large intestine. He determined the relative concentration of βi in his samples of intestinal contents by finding the amount of the sample needed to produce a full contraction of a guinea-pig's uterus when added to Ringer's solution in which the uterus was suspended. He argues that the conditions which he found to favor absorption, namely, an empty intestine and a depletion of the water content of the body, are those presented by infants who have suffered from minor gastro-intestinal upsets, and that they are then liable to severe symptoms due to absorption of βi.

8. Mellenby: Quart. Jour. Med., 1915-1916, **9,** 164.

9. Barger and Dale: Jour. Physiol., 1910, **40,** Proc. 37; ibid., 1910-1911, **41,** 499.

10. Mellanby and Twort: Jour. Physiol., 1912-1913, **45,** 53.

CHRONIC DISTURBANCES OF NUTRITION

Energy Metabolism in Chronic Malnutrition. — Bahrt and Edelstein,[11] and Kurt and Wolff[12] have added to the rather small number of instances in which the energy exchange has been determined in conditions of chronic malnutrition. The infant used in the experiment of Bahrt and Edelstein was 8 months old and weighed 5 kilos. It had suffered a month previously from severe enterocatarrh, following which there was, on breast milk, a steady gain in weight, but when given a modification of cow's milk (⅔ whole milk and 5 per cent. sugar) the gain in weight became irregular and unsatisfactory. The authors define the condition of malnutrition at the time of the experiment as 'Bilanzstörung." The energy exchange was determined by means of a Pettenkofer-Voit respiration apparatus for two periods of four days each, with an interval of four days between. The infant was in the apparatus about twenty-two and one-half hours each day. The infant gained about 60 gm. during each period, which is a normal rate for an infant of 8 months, but is unsatisfactory when the infant is underweight. The nitrogen retention in average for both periods was 0.13 gm. per kilo per day, and about ⅐ of the nitrogen in the food (normal 0.08 gm. to 0.16 gm., or ⅙ to ¼ of intake). The nitrogen retention was therefore barely normal, but much less than would be retained if the previously lost tissue were being rebuilt at a proper rate. Nieman[13] found in the stage of repair following malnutrition a retention of 0.3 gm. per kilo per day, which amounted to 40 per cent. of the nitrogen intake. The energy exchange was nearly identical in both periods. In average for both, of the 121 calories per kilo per day contained in the food, which the authors regard as 60 per cent. more than the normal maintenance need, there was utilized by the organism 112 calories, and of this number 101 were spent in heat production, leaving 11 calories for processes of tissue building. In a normal infant about the same heat value is applied to growth and repair and very much less than 101 calories per kilo per day to actual heat production. Nieman[13] found in the stage of repair following "Atrophie," that 20 of 115 calories per kilo per day utilized by the organism were invested in tissue building, and Rubner and Heubner[14] found in a similar case that 25 of 114 calories were so spent. In both these cases the calories used in heat production were also markedly higher than normal. The authors chose for estimation of the surface area of their infant, Lissauer's modification of Meeh's formula. Their reasons for this choice are not obvious. Lissauer's modification gives a smaller surface

11. Bahrt and Edelstein: Ztschr. f. Kinderh., 1915, **12,** 15.
12. Kurt and Wolff: Jahrb. f. Kinderh., 1913, **78,** (Ergänzungsheft) 1.
13. Nieman: Jahrb. f. Kinderh., 1911, **74,** 663.
14. Rubner and Heubner: Ztschr. f. Biol., 1899, **38,** 315.

area than Meeh's, which in itself contains the tendency, because of the weight factor, to underestimate surface area when applied to undernourished infants. As might be expected from their method of calculation, they obtained for their infant the highest yet recorded value for heat production per square meter of body surface — 1,711 calories. Recalculated by Meeh's original formula, the heat production was 1,475 calories. One thousand calories per square meter may be taken as a maximum average value for the heat production of a normal infant during quiet periods.[15] Bahrt and Edelstein claim that their malnourished infant was extremely quiet throughout the experiment. If this is true, its heat production was about 50 per cent. higher than normal.

Kurt and Wolff measured the energy metabolism of a 4½-months-old infant that had suffered several acute digestive upsets and for some time preceding the experiment had gained only slightly in weight. An occasional rapid loss of weight, sometimes with fever, indicated the presence of a serious derangement of nutritional processes. At the time of the experiment the weight was 3½ kilos. They obtained two periods of four days each with an interval of a week between. The respiratory exchange was measured by a Pettenkofer-Voit apparatus. The food was protein milk with 4 per cent. sugar during the first period and 5 per cent. during the second. During the first period the infant gained 25 gm. and during the second, 70 gm. The stools were loose during the first day of each period, but in the subsequent days were typical "soap stools." That there was no appreciable disturbance of assimilation was suggested by the fact that the nitrogen absorbed was in both periods more than 90 per cent. of the nitrogen in the food. The nitrogen retention was in average of both periods 0.33 gm. per kilo per day, or 31 per cent. of the intake, which is considerably more than is retained by an infant in a normal state of nutrition. During the first period the caloric value of the food was 108 calories per kilo per day. During the second it was 115. The authors regard the caloric intake as 35 to 40 per cent. over the maintenance need of a normal infant. In spite of this apparently liberal supply of extra fuel, there was spent in the processes of metabolism during the first period more calories (123) than the food contained, with the result that 18.6 gm. of body fat were burned during the four days. During the second period the caloric consumption was 111 calories per kilo per day. The heat production per day per square meter of body surface (calculated by Meeh's formula) was, in the first period, 1,581 calories and in the second, 1,431, and was therefore, as in the infant studied by Bahrt and Edelstein, about one half more than

15. Benedict and Talbot: Am. Jour. Dis. Child., 1914, **8**, 1.

periods 0.33 gm. per kilo per day, or 31 per cent. of the intake, which is the amount produced by healthy infants.

The outstanding feature of the results of both of these experiments is the excessive heat production accompanying a chronic disturbance of nutritional processes. The specific dynamic action of protein can scarcely be held accountable for so large an increase in the expenditure of available energy as heat. In the experiment of Bahrt and Edelstein the protein intake was not excessive. The inappropriateness of protein milk as a food in chronic malnutrition is, however, indicated. In the experiment of Kurt and Wolff, the loss of heat by evaporation of water from the lungs and skin was 38 to 44 per cent. of the total heat production (normally 32 to 35 per cent. of the heat produced is so spent). Bahrt and Edelstein's infant lost 23 per cent. in this way. Apparently an anomaly in water metabolism cannot be regarded as a probable cause of the excessive heat production. Bahrt and Edelstein suggest that the extra heat produced must be due either to a primary inability of the organism to build tissue, or else to some cause directly increasing heat production. As regards the first possibility, they hint that a disturbance in the assimilation or subsequent metabolism of some small but essential (therefore probably mineral!) constituent of the food may be at the bottom of the trouble. As a cause for excessive heat consumption they suggest an overactivity of the digestive glands in response to some intra-intestinal stimulus. In view of our complete ignorance of the cause of the energy wastage in malnutrition, it would perhaps be more ingenuous to assume that when the nutritional machinery is out of kilter more heat must be spent in carrying out metabolic processes than when these processes are in exact adjustment.

Energy Metabolism in Absence of the Cerebral Hemispheres.—Talbot[16] determined the energy exchange in an 8-months-old infant in which during an operative search for the cause of its blindness the cerebral hemispheres were found to be absent. Although the infant weighed more than the normal average for its age, its muscular development was extremely poor. Lack of volitional muscular movement was apparently nearly complete. It made few and small movements unless directly stimulated by being touched. Its heat production during four periods in which the slight movements were least frequent, was, in average, 32 calories per kilo per day, and was therefore markedly lower than the average basal metabolism of normal infants (65 calories per kilo[15]). The author regards the low heat output per kilo as due to the relatively small protoplasmic mass within the body from lack of a proper development of muscular tissue by volitional exercise. In pro-

16. Talbot, F. B.: Arch. Pediat., 1915, **32**, 452.

portion to the size of its protoplasmic mass the heat production was in this infant probably normal.

Chronic Malnutrition Due to Protein?—In spite of the nonsuccess of the many attempts which have been made to relate nutritional disturbances to the protein part of infants' food, Benjamin[17] challenges again its reputation for absolute harmlessness. From a lengthy consideration of the existing data and from results of some experiments of his own he is inclined to believe that a prolonged and excessive intake of cow's milk protein may lead to a state of chronic malnutrition characterized chiefly by a slowing of the rate of weight gain. The type of disturbance he describes resembles closely that which Czerny defined as "Milchnärschaden," and for the development of which an excessive amount of fat in the food has usually been blamed. His experiments consisted simply in a determination of the relation of retained nitrogen to gain in weight in a well, and in a malnourished infant. The experiments are unique in the length of period used. The results obtained are interesting, but their interpretation is not obvious, and the indictment of protein which he has devised from them is in the main fanciful. In his first experiment he determined the nitrogen balance in a "nearly normal" infant for closely successive periods of from three to seventeen days and extending from the age of five weeks to 3½ months. The sum of the periods gave a total of seventy days. A metabolism frame being obviously impracticable for such a plan of experiment, he devised a rubber napkin to receive the stools. The infant was given at first breast milk, then breast milk and an increasing amount of skimmed milk, and finally ⅔ whole milk and 5 per cent. sugar. On these three types of milk the average daily gain in weight was in order 16 gm., 24.1 gm., and 13.3 gm., and the average daily nitrogen retention, 0.6 gm., 1.1 gm., and 0.71 gm. Measured per unit of weight gained, the nitrogen retention showed a steady increase as the shift was made from breast milk to cow's milk. For 100 gm. of weight gained, the nitrogen retention was, on breast milk, 3.7 gm., on breast milk and skimmed milk, 4.5 gm., and on ⅔ whole milk and sugar, 5.3 gm. The last two milk mixtures contained nearly double the amount of nitrogen supplied by breast milk alone. With each addition to the nitrogen intake there was noted a rise, and then after a few days a subsidence, of the level of nitrogen retention. A similar experiment was carried out with a six-weeks-old infant that had been misfed since birth, and at the beginning of the experiment weighed only 2,060 gm. It was given breast milk and then breast milk and skimmed milk, the relative and absolute amount of the latter being gradually increased. The total of days during which the nitrogen retention was determined was fifty-

17. Benjamin: Ztschr. f. Kinderh., 1914, **10**, 185.

seven. The average daily gain in weight was, on breast milk, 10 gm., on breast milk and skimmed milk, in moderate amount, 22.5 gm., and with the addition of more skimmed milk, 16.5 gm. The nitrogen retained daily was in order, 0.39 gm., 1.1 gm. and 1.2 gm. Per 100 gm. of weight gained there was a larger increase in the retention of nitrogen as the amount of cow's milk in the food was increased than was noted in the case of the well infant. On breast milk the nitrogen retained per 100 gm. increase in weight was 3.9 gm. As skimmed milk was added it rose to 4.9 and 7.1 gm. The rise in the level of nitrogen retention as the nitrogen intake was increased was fairly sustained. If the 3.7 gm. nitrogen retained by the well infant per 100 gm. of weight gained while receiving breast milk is multiplied by the usual factor, 29.5, the increase in "flesh" thus calculated is 109 gm. Similarly, in the case of the sick infant, while receiving breast milk the calculated gain in "flesh" is 115 gm., which quite fairly approximates the 100 gm. actual gain in weight. With the addition of cow's milk to the diet, and an increase in the nitrogen intake, the actual gain in weight became in both instances greatly less than the increase in "flesh" as calculated from the amount of nitrogen retained. The author regards the correspondence between weight gained and calculated "flesh" increase, obtaining when the infants received breast milk alone and when the nitrogen intake was relatively low, as indicating a normal "correlative" growth; meaning that the newly built tissue contains a normal amount of nitrogen. The "normal" infant, omitting a part of the experimental period during which dyspeptic symptoms were present, gained in weight in fifty-three days 890 gm. The nitrogen retained was 40.6 gm. According to Rubner and Heubner,[18] 0.186 gm. nitrogen may be lost daily in the sweat. Assuming in this case a loss of 0.1 gm. daily, and subtracting 5.3 gm. from the nitrogen retained, the estimated increase in body protein is 1,044 gm. — 154 gm. more than the increase in body weight. The sick infant gained in fifty-seven days 490 gm. and retained 64 gm. of nitrogen. Allowing more liberally in this instance for loss of nitrogen in sweat (0.2 gm. daily) the calculated increase in flesh was 1,550 gm., or more than three times the actual gain in weight. The author spends many pages in contemplation of the riddle of what becomes of the retained nitrogen which is not represented by an appropriate increase in body tissue. A loss of water from the body would permit an equivalent increase in body tissue which would not be indicated by an increase in weight. While admitting the fact that the water content of the tissues decreases as the age of the infant advances, he does not believe that this physiologic loss of water can be made accountable for more than a small part of the discrepancy

18. Rubner and Heubner: Ztschr. f. Biol., 1899, New Series, **37**, 18.

between his actual and calculated figures for body increase. Water retention is known to be a widely fluctuant quantity, but he feels sure that the length of his experimental period rules out the effect of a temporarily low water balance. He does not mention the possibility of a gradual, more than normal, water loss from the malnourished infant, or the possibility of the change in the character of the food producing a change in the water content of the body. He is disinclined for vague reasons to regard a loss of fat as accountable in appreciable degree for his findings. He seems unnecessarily concerned over the possibility of some of the retained nitrogen being applied to repair instead of tissue growth, though it would seem in an experiment of such length that nitrogen used for repair would be covered by the presence in the urine of the effete nitrogen it replaced, and so would not count in the nitrogen balance. His experiments are well planned in point of duration, but whether or not the discrepancy he calculates between tissue increase and nitrogen retention is approximately actual must be regarded as problematical. He mentions that Grafe and Graham[19] encountered a similar dilemma in their study of the ability of the organism to accommodate to continued overfeeding. They found that a healthy dog on a high protein diet retained in fifty-nine days 298 gm. of nitrogen, although its weight, which was 20 kilos, remained stationary throughout the experiment. Benjamin concludes that his results show that a prolonged high intake of cow's milk protein, probably in well infants, and quite certainly in infants whose nutritional processes are already disturbed, leads to the presence in their tissues of an abnormally large amount of nitrogen. Whether the extra nitrogen forms inert deposits or is added to the normal nitrogen content of living protoplasm, its presence in the tissue cells must alter their chemical texture and may therefore with great probability be supposed to interfere with processes of cell metabolism. A slowing in the rate of the processes concerned in tissue building is an effect particularly suspected by the author. The good results obtained by treating chronic disturbances of nutrition of the type of Czerny's "Milchnärschaden" with malt soup he regards as due not to the low fat in this food, but to the small amount of protein present. It would seem that the author's theory of an overstuffing of the tissue cells with nitrogen might be easily tested directly by postmortem tissue analysis.

Organ Analyses in Chronic Malnutrition.—Klose[20] complains that a foundation of chemical facts has never been supplied for the use, in describing disturbances of nutrition, of terms, such as "Dekomposition," for instance, which imply a change in the chemical structure of

19. Grafe and Graham: Ztschr. f. physiol. Chem., 1911, **73,** 1.
20. Klose: Jahrb. f. Kinderh., 1914, **80,** 154.

the organism. The only work previous to his own done to determine the effect of chronic malnutrition on tissue composition is that of Steinert and Weigert.[21] These workers decided from the results of analyses of the bodies of our atrophic infants that, even with the presence of marked emaciation, the normal chemical texture of the tissues is preserved. Their belief is that wasting of body substance is a process in which tissue is lost in toto, and that in the living protoplasm remaining there is no alteration in the relative amounts of the various tissue constituents. Klose believes that such an inference cannot be safely made from the gross results of body analysis. He presents analyses from the individual organs of a 5-weeks-old infant. Before death the symptoms were those of "Mehlnärschaden" and there was marked edema. Figures for comparison were obtained from a new-born infant dying from obstetric trauma. The weights of the two infants were nearly the same — 3,000 and 3,200 gm. He found in the new-born 564 gm. fat and in the atrophic infant only 39 gm. For the body as a whole there was, in 100 gm. fat-free substance, from the new-born 82 gm. water, 14.5 gm. protein and 3.5 gm. ash. Corresponding figures for the atrophic infant were 86 gm., 10 gm. and 2.8 gm. Regarding the excess of water per gram of fat-free dried substance in the atrophic over that per gram of dried substance in the new-born as pathologic, the author estimates that the body of the infant with edema contained more than a liter (1,100 c.c.) of "pathologic" water; 50 per cent. of this extra water was found in the skin and 20 per cent. of it in the muscles. Of the total water content of the new-born, one fifth was found in the skin and one third in the muscles. In the infant with edema this distribution was nearly exactly reversed. The author mentions that in adults only 5 per cent. of the water content of the body is found in the skin and 50 per cent. is in the muscles. There was in the atrophic infant a slightly greater loss of nitrogen than of minerals, as shown by the fact that there was found per gram of nitrogen 1.8 gm. of ash as compared with 1.5 gm. in the new-born. This relatively greater loss of nitrogen is revealed especially in the skin and muscles. As regards the individual constituents of the ash, there was found more sodium and chlorin and less calcium, magnesium, and especially potassium, in the infant with edema than in the new-born. The increase in sodium and chlorin did not seem to be especially related to the water retention, since the increase was most marked in the muscles, whereas most of the extra water was found in the skin. The relative amounts of the various minerals in the skin, muscles and viscera was found to differ more or less from the proportions obtaining in the new-born. The ratio of calcium to magnesium in the muscles,

21. Steinert and Weigert: Monatsch. f. Kinderh., 1905, 4, 301.

for instance, was found to be the reverse of normal. The author concludes that the results of his chemical autopsy thoroughly disprove the theory of a "constancy of the relative composition of tissue" advanced by Steinert and Weigert.

ACIDOSIS

Keller,[22] in 1896, reported a marked increase in the "ammonia coefficient" (ammonia nitrogen to total nitrogen in the urine) in cases of severe nutritional disturbance in infants. In many instances he found more than 50 per cent. of the urinary nitrogen in the form of ammonia. He used the old and very inaccurate Schlösing method, and much of the ammonia he measured must have come from decomposition of urea. Nevertheless, the fact that the ammonia coefficient may be high in cases of disturbed nutrition has since been well substantiated. During the twenty years since Keller reported this finding there has been from time to time a great deal of discussion in the literature as to the source and significance of this increased urinary ammonia. Pfaundler[23] believed that in cases of malnutrition, as part of a general lowering of the oxidative ability of the tissues, the liver was unable to synthesize urea to the normal extent, but the early observation of Bergh,[24] who found that the ammonia could be made almost entirely to disappear from the urine by giving sodium bicarbonate, pointed strongly to the inference that the extra ammonia in the urine represented an unusual need on the part of the body to conserve its supply of fixed alkali, and this interpretation of the finding came to be the generally accepted one. Pfaundler himself later suggested the word "Alkalopenie" to describe the condition represented by an increase in urinary ammonia. Recent research has shown this term of Pfaundler's to be absolutely accurate. The term acidosis was frequently applied to the condition, but always with a certain diffidence because of the usual absence of the ketone acids which regularly accompany the high ammonia coefficient in diabetic acidosis. Search for other organic acids was unsuccessful.[25] Finkelstein made the easy assumption that the extra base was needed to neutralize acid products of bacterial fermentation absorbed from the intestine, but supplied no chemical facts in support of his view. Steinitz[26] by showing that infants receiving a milk high in fat lost an unusual amount of sodium and potassium in the stools (coincident with an increase in the ammonia in the urine), and the finding by other workers of a frequently negative mineral balance, especially for sodium and potassium, in diarrhea, led finally

22. Keller: Jahrb. f. Kinderh., 1897, **44,** 25.
23. Pfaundler, M.: Jahrb. f. Kinderh., 1904, **60,** 719.
24. Bergh, van den: Jahrb. f. Kinderh., 1897, **45,** 265.
25. Statement by Steinitz: Monatsch. f. Kinderh., 1902, **1,** 225.
26. Steinitz: Jahrb. f. Kinderh., 1903, **57,** 689.

to a definite belief that a high ammonia coefficient, if unaccompanied by acetonuria, indicated a "relative" acidosis; that is, the acidosis was caused by a loss of base and not by the presence of abnormal acids, as in the "true" acidosis of diabetes. All of the work which supports this belief contains the fallacy pointed out by Howland and Marriott[27] that the loss of acid radicals was not determined and shown to be less than the loss of base. As regards the actual disability which the organism may suffer from such a "relative" acidosis, opinion has been entirely vague. All attempts to supply infants showing a high ammonia coefficient with a distinguishing set of clinical symptoms have been unsuccessful.[2] General opinion seems to have been to regard the "relative" acidosis as probably completely compensated for by the extra ammonia supplied by the body at the expense of urea, and not in itself a serious condition. This is evidenced by the single fact that there has been no tendency to treat the condition by giving alkali. Czerny[28] alone suspected correctly that the deep breathing which he observed in certain cases of severe diarrhea was related to a serious disturbance of the acid-base equilibrium within the body. He was led to this inference because of the resemblance of the type of respiration to that shown by rabbits poisoned with mineral acids.

The mechanism by means of which the neutrality of the blood is maintained has been uncovered for us with wonderful clearness by the work of L. J. Henderson.[29] Recently, methods have been devised for testing directly the efficiency of the parts of this mechanism. The presence of a condition which may correctly be called acidosis need therefore be no longer a matter of uncertain inference, based, for instance, on the presence of the ketone acids, or of an unusually large amount of ammonia in the urine. It is a regular function of ammonia to save alkali for the body. A high ammonia coefficient merely means an unusual need for alkali conservation, but does not in itself afford ground for supposing that the body's store of fixed alkali is actually reduced. As regards the acetone bodies, the neutrality mechanism is capable of an adjustment which will manage the conveyance of large amounts of these abnormal acids into the urine without depletion of the normal alkali content of the blood. It is therefore absolutely improper to regard the presence of acetone bodies in the urine as proof of a disturbance of the acid-base balance within the body. With our new knowledge and methods, the terms acetonuria and acidosis need no longer be jumbled. By acidosis we understand an embarrassment of the neutrality mechanism due to a less than normal alkali content of

27. Howland and Marriott: Am. Jour. Dis. Child., 1916, **11**, 309.
28. Czerny: Jahrb. f. Kinderh., 1897, **45**, 271.
29. For a summary see Henderson: Ergebn. d. Physiol., 1909, **8**, 254.

the blood and of such degree that it has caused the reaction of the blood to slip slightly in the direction of acidity. The increase in the hydrogen ion concentration in the blood is always extremely small. A shift from the normal slightly alkaline reaction to only so far as neutrality is not compatible with life. The increase in acidity is usually so small that it cannot be directly measured by our present methods. The respiratory center, however, is sensitive to an almost infinitesimal increase in the hydrogen ion concentration in the blood and promptly and definitely indicates its presence by causing an increased ventilation of the alveolar air spaces. This response of the respiration center is visible clinically as hyperpnea and is demonstrable chemically by the finding of a lower than normal CO_2 tension in the alveolar air, due to the dilution of the alveolar air produced by the extra ventilation. The physiologic purpose of the lowering of the CO_2 tension in the air spaces is to produce a corresponding decrease in the carbonic acid content of the blood in effort to restore there the normal ratio between acid and base which is disturbed in acidosis by a reduction of the blood's fixed alkali content. The presence of an acidosis can therefore be definitely shown by finding, (1) a lower than normal CO_2 tension in the alveolar air or in the blood, or (2) a lower than normal alkali content of the blood or, (3) an increase in the hydrogen ion concentration of the blood.

Using the most recent methods, Howland and Marriot[27] have shown with great thoroughness that infants with diarrhea may develop an actual and extremely dangerous acidosis. The urine of these infants does not contain acetone bodies in significant amount. The only clinical symptom which regularly accompanies the acidosis and is a reliable guide to its presence is deep breathing — hyperpnea — accomplished by vigorous use of the thoracic as well as of the diaphragm muscles. With the help of an ingenious mask they were able by the Plesch method to collect, for the first time from infants, alveolar air samples. In a series of normal infants they found the carbon dioxid tension to vary from 36 to 45 mm. In infants severely sick with diarrhea and showing hyperpnea, the carbon dioxid tension was always below 30 mm., often below 20 mm., and in one instance was only 14 mm. By a simple method which Marriott[30] has devised they were able to demonstrate a well-marked reduction of the alkali content of the blood serum in these cases. The method consists in blowing out the carbon dioxid from the serum and then reading the hydrogen ion concentration by the indicator method of Levy, Rowntree and Marriott.[31] After removal of the volatile fraction (carbon dioxid)

30. Marriott, W. McK.: Arch. Int. Med., 1916, Part 1, **17,** 840.
31. Levy, Rowntree and Marriott: Arch. Int. Med., 1915, **16,** 389.

of the acid content of the blood its reaction will necessarily shift in the direction of alkalinity, and the shift will be large or small according as there is much or little base present. They found that normally the reaction of the serum after removal of the carbon dioxid is, using the logarithmic notation for hydrogen ion concentration, between 8.4 and 8.5. In their cases of diarrhea with hyperpnea it ranged from 8.1 to 7.5. (In the logarithmic notation the numerals decrease as the hydrogen ion concentration increases.) Testing the serum directly, without first removing the CO_2, they were able to measure by the indicator method, in some of their cases, an actual very slight increase in the hydrogen ion concentration. In normal infants the reaction of the serum was never more than 7.4. In diarrheal cases with hyperpnea they several times found the hydrogen ion concentration increased to 7.2. They were also able to show indirectly but more strikingly the presence of an actual increase in the hydrogen ion concentration of the blood by testing the oxygen combining power of its hemoglobin by the method of Barcroft.[32] Barcroft has determined that if normal blood is exposed to an oxygen tension of 17 mm., in the absence of CO_2 the hemoglobin becomes 70 to 80 per cent. saturated; but that if the acidity of the blood is very slightly increased, much less oxygen is combined. Howland and Marriott found that blood from their cases of diarrheal acidosis became, when exposed to a tension of 17 mm. of oxygen, only 15 to 25 per cent. saturated. The evidence advanced by Howland and Marriott to show that a dangerous acidosis may be present in diarrhea is remarkably complete and definite, and as it supplies an obvious therapeutic indication — the administration of alkali — the finding is one of immense usefulness. The cause of the reduction of the alkali content in the blood in these cases is at present entirely obscure.

ACETONURIA

That the acetone bodies are regularly present in small amounts in the urine of normal infants and children has been repeatedly shown. Langstein and Meyer[33] found 1 to 4 mg. in twenty-four-hour urines from infants, and in older children 3 to 10 mg. Liefman[34] gives approximately the same figures. Veeder and Johnson[35] have recently examined the urines from twenty-one normal infants and children for acetone and diacetic acid, and for beta-oxybutyric acid using the more recent method of Schaffer. They found a much larger amount of acetone bodies than had been previously reported. Expressed as acetone, the average daily excretion was 50 to 80 mg. Slightly more

32. Barcroft: The Respiratory Function of the Blood, 1914, Cambridge.
33. Langstein and Meyer: Jahrb. f. Kinderh., 1905, **61,** 438.
34. Liefman: Jahrb. f. Kinderh., 1913, **77,** 125.
35. Veeder and Johnson: Am. Jour. Dis. Child., 1916, **11,** 291

than half was usually in the form of beta-oxybutyric acid. Hüssy[36] obtained an enormous increase in acetone excretion in children by placing them on a fat and protein diet. The acetone in the urine increased rapidly and in several instances amounted to more than a gram on the second day of the diet. Other observers have also found that infants and children are much more liable to an acetonuria from carbohydrate deficiency in the diet than are adults. It has been suggested that the reserve supply of carbohydrate in the younger organism is relatively small. L. Meyer[37] measured a quite considerable increase in acetone excretion in acute infectious diseases. In measles and scarlet fever he found as much as 140 mg., and in diphtheria 160 mg. He assumes the increase to be due to inanition and probably more directly to an insufficient carbohydrate intake. That there is very frequently an increase in the acetone excretion in infants and children beyond the amount which may be called physiologic has been well indicated by Howard.[38] He examined the urine from 171 consecutive patients suffering from various minor ailments and found that in thirty-one instances there was enough acetone present to make positive the rather insensitive sodium nitroprussid test. Digestive upsets and acute infections of a not very serious type, such as tonsillitis, coryza, otitis media and bronchitis were the conditions most often accompanied by a positive acetone test. Metcalf,[39] in studying a curious epidemic among infants and children in Concord, Mass., in which the symptoms suggested food poisoning, found acetone present in all of the cases (100) in which the urine was examined. Acetonuria may apparently be regarded as a disease symptom occurring in infancy and childhood nearly as frequently as fever. The assumption, however, that its presence always indicates a dangerous defect in metabolism, namely, acidosis, is quite unjustifiable. The papers of Metcalf and Howard, and others which might be cited, bear in their titles the word acidosis, but contain no evidence to show that the acid-base balance in the body is actually disturbed by the presence of these abnormal acids. The fact that the ferric chlorid test was negative in two of Metcalf's five fatal cases would suggest that the ketone acids were probably not present in an amount sufficient to embarrass the neutrality mechanism, and that these children quite certainly did not die of acidosis.

PERIODIC VOMITING

Very little investigative work in this condition has appeared in recent years. An experiment of Hilliger's[40] may be described. The

36. Hüssy: Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs., 1906, **1,** 5.
37. Meyer: Jahrb. f. Kinderh., 1905, **61,** 438.
38. Howard: Boston Med. and Surg. Jour., 1915, **172,** 747.
39. Metcalf: Am. Jour. Dis. Child., 1915, **9,** 28.
40. Hilliger: Jahrb. f. Kinderh., 1914, **80,** 1.

subject was a 6-year-old girl suffering from quite typical attacks of periodic vomiting. The author's chief point is that he was able to induce attacks by lowering the carbohydrate portion of the diet. He gave a normal diet containing 36.5 protein, 52 gm. fat, and 160 gm. carbohydrate, and on this found that the acetone bodies in the urine amounted to 4 to 5 mg. daily. An addition of 100 gm. fat to this diet caused a scarcely appreciable increase in acetone excretion (5.9 mg.); but when the carbohydrate intake was reduced by half — to 75 gm. — the acetone in the urine rose on the same day to 134 mg., on the next day to 640 mg., and on the day following fell to 423 mg. On the fourth day the acetone in the urine was again the normal amount. During the three days that the acetone in the urine was high the child suffered a vomiting attack with typical symptoms. A diet similarly low in carbohydrate was given to several normal children, but did not cause an increase in acetone exretion. The experiment was repeated on the susceptible subject and a nearly identical increase in the acetone excretion for a period of three days was obtained. This time the blood sugar was determined each day by the Bang micromethod and was found on the second day of the attack to be decreased by one half. The figures for blood sugar on the three successive days of the attack were 0.13, 0.07 and 0.13 gm. per 100 c.c. The amount of acetone in the urine during these days was 175, 620 and 200 mg. On the second day of the attack the vomiting and other symptoms were most severe. The author points out that the symptoms abated and the acetone in the urine came down to normal before the usual carbohydrate intake was restored (the child took almost no food during the three days), and that therefore the attack cannot be referred to an insufficiency in the body of stored carbohydrate. His interpretation, based on the finding of a low sugar content of the blood on the second day, is that the demand for the release of carbohydrate from its storage depots created by the insufficient carbohydrate intake, is less quickly met than is normally the case. As soon as the sugar mobilization mechanism gets under way and supplies the processes of intermediary metabolism with a proper amount of carbohydrate, as indicated by the presence of a normal amount of sugar in the blood on the third day, all evidences of metabolic disturbance disappear. The author's theory is ingenious and interesting, but rests rather heavily on a single blood sugar determination.

RICKETS

In spite of numerous and laborious investigative attempts, not the slightest hint of the character of the error in metabolism which causes the condition of rickets has yet been obtained. All feeding or gland extirpation experiments have yielded negative results or have led only

to the production of the ubiquitous osteoporosis — a condition in which bone is more or less empty of calcium, but does not present histologically a trace of the changes which are characteristic of rickets. As regards calcium metabolism in rickets, little more has been learned than might be expected from the histologic picture. The calcium content of rachitic bone is much lower than in normal bone. Schabad found, for instance, that ribs from normal infants contained 22 to 25 gm. CaO, whereas in ribs from rachitic infants there was 4 to 17 gm. CaO. Aschenheim[41] analyzed for calcium the ash of blood obtained postmortem from rachitic children and found a widely variable Ca content, ranging in a series of seventeen cases from 3.7 to 12.8 mg. CaO per 100 c.c. of blood. In a series of normal infants he found a fairly constant value of 8 to 10 mg. per 100 c.c. He interprets his findings as meaning that in rickets calcium is lost from the bones and turned into the blood at an irregular rate. Katzenellenbogen,[42] using the micromethod of Wright, by which the amount of ionized calcium in the blood is roughly indicated by determining the amount of ammonium oxalate which must be added to the blood to prevent its clotting, could not find that the Ca content of the blood in any of the stages of rickets differed from that in the blood of normal infants. A reliable method for measuring calcium in the ash of small blood samples has been at last supplied by Marriott and Howland.[43] Using this method they found in three samples from placental blood, and in the blood of six normal infants and three adults, a remarkably constant amount of calcium.[44] Except in one instance, the amount of Ca per 100 c.c. of serum was between 9.8 and 11.3 mg. They examined blood from eleven infants under 1 year of age showing clinically evidence of active rickets, and found that in some of the cases the calcium in the blood was slightly reduced, but in no instance did they find less than 9.0 mg., and in five of the cases the Ca content was more than 10 mg. Aschenheim and Kaumheimer[45] have recently shown that the amount of calcium in the muscles of rachitic children is less than normal. Numerous experiments have shown that in the florid stage of rickets the amount of calcium daily retained is nearly always below the average normal figure of 0.17 gm. CaO, supplied by Orgler.[46] Not infrequently the Ca balance is negative. The immediate suggestion of the lowered Ca balance, that rickets might be due to a primary calcium insufficiency, as might occasionally happen in breast fed infants, or to a secondary

41. Aschenheim: Jahrb. f. Kinderh., 1914, **79,** 446.
42. Katzenellenbogen: Ztschr. f. Kinderh., 1913, **8,** 187.
43. Marriott, Howland and Haessler: Jour. Biol. Chem., 1916, **24,** Proc., **18.**
44. Howland and Marriott: Tr. Am. Ped. Soc., 1916, **28,** 200.
45. Aschenheim and Kaumheimer: Monatsch. f. Kinderh., 1912, **10,** 435.
46. Orgler: Ergebn. d. inn. Med. u. Kinderh., 1912, **8,** 166.

insufficiency due to an interference with calcium absorption, by excessive formation of soap stools for instance, seems unlikely, since in all experiments in which these conditions have been imitated the only result has been the occasional production of an osteoporosis. The low or negative calcium balance is therefore much more probably due to some defect in its intermediary metabolism which prevents its deposition in bone tissue. The amount of calcium retained increases, and often becomes much higher than normal, during the healing stage of rickets. The administration of codliver oil, calcium salts and preparations of organically combined calcium have been found to cause an increase in calcium retention. They may therefore be fairly regarded as remedial agents. Whether their effect is to cause an increased absorption of calcium or in some way to mend the defect in its intermediate metabolism, is not apparent. Schloss[47] has recently completed a long series of laborious experiments in which he determined the effect on calcium retention in rachitic children of the administration of cod liver oil and of calcium preparations, alone and together. The effect was tested in infants on breast milk, on a milk high in fat, and on protein milk. His results in average from a series of eighty experiments were as follows: Calcium retention in the fore-period was 0.032 gm. CaO per day. Cod liver oil alone produced an average daily retention of 0.167 gm. Calcium preparations alone gave a retention of 0.297 gm. daily. When both cod liver oil and calcium preparations were given, the average daily retention of CaO was 0.354 gm. He gave the cod liver oil with and without phosphorus without being able to notice a difference in its effect on calcium retention. Tricalcium phosphate caused a slightly better retention than calcium acetate and was equally as efficient as various preparations containing organically combined calcium. In a number of his experiments he measured also the retention of the other minerals, sodium, potassium and magnesium. It has been noticed that as the calcium retention increases in healing rickets the retention of sodium and potassium falls and may become negative. From this a relation of the alkaline minerals to rickets has been inferred, and the observation has also been much mentioned as an instance of an "antagonism" which is supposed to exist between the metabolism of the earth alkalies and of the alkaline minerals. Schloss was able to show that the reduction of Na and K retention is probably due merely to an interference with their absorption, caused by the stimulus to peristalsis provided by cod liver oil. He found that when protein milk, which prevented this effect of cod liver oil, was given there was no disturbance of alkali retention. He also made the interesting observation that during the florid stage of rickets there was in

47. Schloss: Jahrb. f. Kinderh., 1915, **82**, 435.

some instances an abnormally high magnesium retention, which fell rapidly to a low or negative value during the healing stage, and as the calcium retention increased. He is, however, in doubt as to whether this finding may not in some way be related to the medication given.

OSTEOGENESIS IMPERFECTA

The metabolism of calcium in this condition has been studied by several workers. Schwarz and Bass[48] found in a 7-months infant an average daily retention of 0.109 gm. CaO. In a 3-months infant, Bamberg and Huldschinsky[49] found in average 0.042 retained daily. An average from three periods during which the infant received cod liver oil and phosphorus gave a daily retention of 0.089 gm. Bookman,[50] studying an infant of the same age, found a daily retention of 0.054 gm. CaO and was able to increase the retention to 0.402 gm. by giving calcium lactate in the food. Orgler[46] gives the daily retention of CaO in normal infants as ranging from 0.13 to 0.21 gm. CaO. The results of the experiments just cited suggest that calcium retention is somewhat low in osteogenesis imperfecta during infancy, and that an increase in retention may be obtained by giving calcium salts (evidence of a single period obtained by Bookman). Schabad[51] determined the calcium balance in an older child in twelve six-day periods between the ages of 7 and 10 years. There was unfortunately only one period without medication; this gave a calcium balance of 0.176. Two periods with phosphorus and cod liver oil gave a balance of 0.340. In a period during which she received calcium acetate and cod liver oil the daily retention was 0.338 gm., but for another period with the same medication the balance was slightly negative. Two periods in which thyroid extract was given, gave in one a low (0.047 gm.) and in the other a slightly negative balance. During two periods with Fowler's solution there was retained 0.403 gm. and 0.382 gm. Herbst[52] found in a normal child of this age 0.418 CaO retained daily. Schabad concludes that calcium retention is low in osteogenesis imperfecta and can be best restored to normal by giving arsenic. His results, however, give the impression strongly that the amount of calcium retained varied widely and probably without relation to the kind of medication given.

TETANY[53]

Because of the frequent association of tetany with rickets, investigation early took the direction of attempts to show a disturbance of

48. Schwarz and Bass: Am. Jour. Dis. Child., 1913, **5,** 131.
49. Bamberg and Huldschinsky: Jahrb. f. Kinderh., 1913, **78,** (Ergänzungsheft), 241.
50. Bookman: Am. Jour. Dis. Child., 1914, **7,** 436.
51. Schabad: Ztschr. f. Kinderh., 1914, **11,** 230.
52. Herbst: Jahrb. f. Kinderh., 1912, **76.**
53. For fairly recent reviews of literature of tetany see Rye: Arch. Pediat., 1914, **31,** 664, and Aschenheim: Jahrb. f. Kinderh., 1914, **79,** 446.

calcium metabolism. Stoeltzner,[54] from feeding experiments in which he gave calcium salts, decided that tetany was due to an increase in the calcium content of the tissues. This view is probably the mirror image of the truth in the matter. Numerous experiments have failed to show that a negative or decreased calcium balance occurs with any regularity in tetany. Quest,[55] however, found the calcium content of the brains of two infants with tetany very considerably lower than that of the brain of a normal infant. Assuming the nitrogen content to be constant, he found that the ratio N : Ca was in the brain from the normal infant 164, while in the brains from the spasmophilic infants the quotient was 240 and 269. Ramacci[56] and Silvistri[57] also found less than the normal amount of calcium in brains from spasmophilic children. M. Cohen,[58] however, was not able to confirm this finding. Pollini[59] found in analysis of the ash of blood obtained postmortem from three cases of tetany, 2.0, 2.7 and 3.8 mg. of CaO per 100 c.c. The blood of his single control patient, however, contained only 2.3 mg. These figures are far below the average for normal infants — 8 to 10 mg. — supplied by Aschenheim.[41] Katzenellenbogen,[42] using the micromethod of Wright, which measures roughly the ionized calcium in the blood, found on examining the blood of five infants with tetany that in four of them the method occasionally indicated that there was less than the normal amount of calcium present. Definite information on this point has been very recently supplied by Howland and Marriott.[44] They used a micromethod for ash analysis devised by themselves and found the calcium content of the blood in tetany to be regularly low. In seven cases with active symptoms the Ca content of the blood was found to be 5.0 to 6.5 mg. per 100 c.c., except in one instance in which it was 7.3. In a case in which tetany was latent, that is, was indicated only by the presence of characteristic electrical reactions, there was found in the blood 8.5 mg. Ca. In one of the cases which gave, during the presence of active symptoms, a Ca content of 6.0 mg., there was subsequently found, after the disappearance of all evidences of tetany, 10.4 mg. Ca. In blood samples from five normal infants the amount of Ca was found to lie between 10.8 and 11.5 mg. per 100 c.c. They found also in tetany in dogs following removal of the parathyroids, a decrease in the calcium content of the blood. In one instance, before operation the Ca in the blood was 10.8 mg., and forty-eight hours after parathyroidectomy was 7.3 mg. In another experiment the Ca content

54. Stoeltzner: Jahrb. f. Kinderh., 1906, **63,** 661.
55. Quest: Monatsch. f. Kinderh., 1911, **7.**
56. Cited by Aschenheim, note 53.
57. Cited by Aschenheim, note 53.
58. Cited by Aschenheim, note 53.
59. Cited by Aschenheim, note 53.

before operation was 10.0 mg., and twenty hours after was 8.9. Six days after the operation it had fallen to 6.8 mg.

The finding by physiologists that certain mineral ions exert a specific effect on nerve muscle irritability has greatly stimulated investigation of the cause of tetany. J. Loeb[60] designates nerve muscle irritability as a function of the quotient Na ÷ Ca; Na tending to decrease and Ca to increase the threshold for excitation. The ion K has been credited with the same property in this respect as Na, whereas Mg has been shown by Melzer to exert a depressant effect similar to that of Ca. Neuromuscular hyperirritability would therefore seem to be due to a disturbance in the balance normally maintained between the antagonistic effects of the earth alkali ions Ca and Mg on the one hand, and the alkali ions, Na and K on the other, and in the direction of producing an abnormal preponderance of the specific effect exerted by the alkalies. The effect of administration of salts containing these various mineral ions in the condition of tetany has been tested by a number of workers. Rosenstern[61] was able to demonstrate in children with tetany a reduction of electrical irritability after giving large amounts of calcium salts by mouth; and after giving 6 to 8 gm. of NaCl he thought that an aggravation of the tetanoid condition could be observed. He noted an improvement when whey was withdrawn from the diet. Zybell[62] was also able to reduce slightly electrical irritability in tetany by giving large amounts of calcium salts, and to increase it by giving a single dose of 3 gm. of potassium acetate. Grulee,[63] using smaller doses of calcium, obtained no effect. Berend[64] finds that injection of magnesium sulphate reduces electrical hyperirritability and relieves carpopedal spasm. MacCallum and Voegtlin[65] found that, in the case of dogs with tetany produced by parathyroidectomy, the injection of calcium or of magnesium salts stops the tetanoid symptoms, whereas the injection of sodium or potassium salts tends to increase their severity. This latter effect is, however, not so clear cut as the opposite one exerted by Ca and Mg. If the theory that the hyperirritability in tetany is due to a preponderance of the specific ion effect of the alkalies, Na and K, over that exerted by the earth alkalies, Ca and Mg, is accepted, it may be assumed that the alkalies are absolutely increased, or that they are only relatively in excess, due to the presence of a less than normal amount of Ca + Mg in the tissues. In favor of the latter view is the finding of Quest that the Ca content of the brains of spasmophilic children is low. This

60. Cited by Rye, note 53.
61. Rosenstern: Jahrb. f. Kinderh., 1912, **62,** 154.
62. Zybell: Jahrb. f. Kinderh., 1913, **78,** 29.
63. Grulee: Am. Jour. Dis. Child., 1913, **5,** 205.
64. Berend: Monatsch. f. Kinderh., 1913, **12,** 269.
65. MacCallum and Voegtlin: Jour. Exper. Med., 1909, **11,** 118.

has been confirmed by Cooke and others. McCallum and Voegtlin found the amount of calcium in the brain, spinal cord and blood of dogs with parathyroid tetany abnormally low. They speak of tetany as "calcium diabetes." Very definitely to the point is the low calcium content of the blood of infants with tetany, recently shown by Howland and Marriott. Unfortunately, nothing is known quantitatively of the metabolism of magnesium in tetany. Aschenheim,[66] although he found a less than normal amount of calcium in the brains of spasmophilic children, claims, however, that there is also an absolute increase (Stauung) of the alkalies in the brain tissue. He is inclined to relate tetany to an abnormally high sodium and potassium retention and advocates a complete removal of whey from the milk for relief of the condition. Lust[67] describes the case of a child of 2 years with marked edema and tetany, which disappeared when the edema was relieved, and infers that the tetany was due to an increased NaCl retention. This observation of Lust has led Brown and Fletcher[68] to formulate a theory of the cause of tetany which refers the condition to an increase of Na and K in the tissues, due to an increased water retention which has been brought about by overfeeding with carbohydrate. They also regard constipation as an important factor in causing an abnormally high retention of the alkaline minerals, arguing this inversely from the relatively large loss of Na and K, as compared with Ca and Mg, in diarrheal stools shown by Holt, Courtney and Fales.[3] In support of their theory they present the results of a single experiment with a 13 months infant with tetany. They determined the retention of Na, K, Ca and Mg for two five-day periods. During the first period the infant was extremely constipated and the twenty-four hour amount of urine was less than 200 c.c. Before and during the second period a diuresis was produced by the administration of urea by mouth, the twenty-four hour amount of urine increasing to 600 c.c. The infant was less constipated during the second period, electrical irritability was much lower and carpopedal spasm had disappeared. In the second period as compared with the first, there was a decrease in the amount of K_2O retained, 0.2202 as against 0.4464 gm. and a marked increase in the retention of MgO, 0.0706 gm. as compared with 0.0032 gm. in the first period. The amounts of Na_2O and CaO retained were practically the same in both periods; the figures for Na_2O were 0.143 gm. and 0.145 gm., and for CaO, 0.3896 gm. and 0.4389 gm. There was therefore, an increase in the earth alkalies and a decrease in the alkalies in which sodium did not share. How the authors construe their results to support the view that tetany is caused chiefly by an unusual retention of sodium and

66. Aschenheim: Monatsch. f. Kinderh., 1910, **9**, 366.
67. Lust: München. med. Wchnschr., 1913, **6**, 93.
68. Brown and Fletcher: Am. Jour. Dis. Child., 1915, **10**, 313.

potassium is not obvious. Whether or not tetany should be referred to a disturbance of function in the parathyroid gland is a difficult point and remains unsettled. The physiologic and chemical findings in tetany in infants and in experimental animals after parathyroidectomy are nearly identical. Histologic evidence is, however, quite definitely negative as regards an association of the parathyroid with tetany in infancy, but it is of course not permissible to conclude from the absence of morphologic change that there can be no disturbance of chemical function.

Quite new and interesting chemical findings in tetany after parathyroidectomy have recently been reported by Wilson and co-workers.[69] They have shown that in dogs after removal of the parathyroids there develops a disturbance in the acid-base balance in the body to the extent of causing a shift in the reaction of the blood in the direction of alkalinity. The condition which results may therefore be termed alkalosis. They demonstrated its presence very thoroughly by finding an increase in the carbon dioxid tension in the alveolar air, an increased saturation of hemoglobin with oxygen and also by measuring directly a slight decrease in the hydrogen ion concentration in the blood. Additional evidence was obtained by determining a decrease in the titratable acid, ammonia, and hydrogen ion concentration in the urine. All of this evidence of alkalosis disappeared during the periods of acute tetany, probably because of the production of lactic acid accompanying the muscular spasms. The alkalosis could be made to disappear by the injection of hydrochloric acid. They made also the extremely interesting observation that the injection of calcium salts not only relieves the symptoms of tetany, as was shown by McCallum and Voegtlin, but also that following its administration there is a change in the reaction of the blood in the direction of acidity, as shown by a decreased combining power of hemoglobin for oxygen and a lowering of the tension of carbon dioxid in the alveolar air, just as is obtained after the injection of acid.

SCORBUTUS

Bahrt and Edelstein[70] analyzed the ash of the bones and organs from an 8 months infant dying with scorbutus. They found in the bones one fifth to one third as much calcium as normal, and a parallel decrease in the amount of phosphorus. This finding is identical with that which obtains in rickets, and, moreover, they found, as in rickets, a low calcium content in the muscles. For the results of their alkali analyses of bones, good comparison figures are lacking, but the authors

69. Wilson, Stearns and Thurlow: Jour. Biol. Chem., 1915, **23,** 89. Wilson, Stearns and Janney: Jour. Biol. Chem., 1915, **21,** 169, and 1915, **23,** 123.

70. Bahrt and Edelstein: Ztschr. f. Kinderh., 1913, **9,** 415.

believe that the amounts of sodium and potassium found were at least as much as normal. The bones contained one half as much dried substance as normal, and two to three times as much water. They are inclined to regard the figures obtained from analysis of the ash of the viscera as probably normal, although satisfactory data for comparison does not exist. The authors refrain from stating definitely that the infant was not rachitic.

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